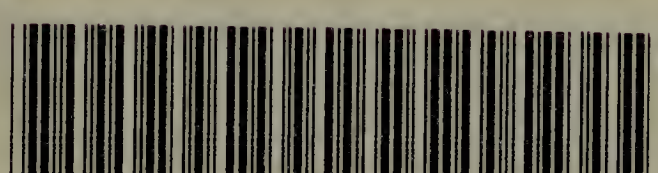


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The Lettsomian Lectures

ON

DYSENTERY

Delivered before the Medical Society of London, 1914

BY

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The Lettsomian Lectures

ON

DYSENTERY.

LECTURE I.

THE HISTORY OF DYSENTERY.

Life is short and the Art long ; the opportunity is fleeting ; experiment is dangerous and decision is difficult. The physician must not only be prepared to do what is right himself, but also to make the patient, the attendants, and externals coöperate.—*1st Aphorism of Hippocrates.*

GENTLEMEN,—I should like in the first place to express my full appreciation of two compliments paid to me by the President and Council of the Medical Society : the original invitation to deliver the Lettsomian lectures for this year, and the gracious courtesy which has permitted the postponement of their delivery for reasons of health which were beyond my own control.

I imagine that it is the duty of the lecturer to choose a subject about which he believes himself to be less ignorant than about others, and at the same time to select a theme which is of some practical importance to many Fellows of this society. Every year a considerable number of cases of uncured dysentery is imported into Great Britain, sometimes open and avowed, often masked and silent, but always of some potential danger to the community. Another reason for inducing me to select this topic is that I find since this lectureship was established in 1850 dysentery has only once been taken as the subject of the lectures. In 1881

Sir Joseph Fayrer, K.C.S.I., F.R.S., lectured here on Tropical Dysentery and Diarrhœa, and though his lectures did not appear in the Transactions of the Medical Society nor in the medical journals of the time, they were reproduced with some other papers in book form at the end of 1881.

It is instructive now to take stock of the knowledge gained of the diagnosis and treatment of dysentery during the 33 years which have intervened. The history of the disease shows us that, almost more than any other infectious disorder, it has had a widespread diffusion all over the inhabited world; most countries have suffered from national visitations, and it is still true that wherever man is found some form of it is liable to appear.

Although there is no evidence to show that our insufficiently clad, fruit-loving, prehistoric ancestors were plagued by dysentery, Hindu records carry us back some 3000 years, to the time when the disease was sufficiently well known to be divided into acute and chronic varieties, and therefore named differently. The Hindu surgeon Sushruta,[1] who lived three or four centuries B.C., was by no means ignorant of preventive medicine, for he wrote: "He falls an easy victim to internal and external diseases who drinks of, or bathes in, a pool of water which is full of poisonous worms, or is saturated with urine or fæcal matter, or is defiled with germs of vermin or decomposed animal organisms, or is covered over with the growth of aquatic plants, or is strewn over with withered and decomposed leaves, or which in any way is rendered poisonous and contaminated, as well as he who drinks and bathes in the freshly collected water of a pool or a reservoir during the rains."

To great Hippocrates seems to belong the credit of the name dysentery and of differentiating it from diarrhœa, though we see by his aphorisms that he was quite aware of the possible transition of one disease into the other. He knew that dysentery was more likely to be fatal to children between 5 and 10 years of age than to adults, and another aphorism says: "If, in a person ill of dysentery, substances resembling flesh be discharged from the

bowel it is a mortal symptom." He pointed out the danger of such symptoms as fever, thirst, and inflammation of the liver or stomach; "the more of these symptoms there are, the greater the danger; and the fewer, the more hope is there of recovery."

Dysentery was well known to all later writers of antiquity. Celsus, for instance (Lib. IV., Sect. XV.), tells us that there are in the interior of the intestines ulcers from which blood flows, mixed with fæces or mucus; that the patient suffers continuously from tenesmus and pain near the anus, and that if the case becomes chronic it is wise to administer soothing enemata. He devotes another paragraph to "the disease called by the Greeks tenesmus," but says that it may be treated like dysentery. Dr. Budge[2] has just translated from Syriac into English a series of lectures on human anatomy, pathology, and therapeutics, which were originally written in Greek by a learned and distinguished, but unnamed, physician who had evidently studied in Alexandria when that city was the scientific centre of the world. The author was an earnest follower of Hippocrates, and his lectures were translated from Greek into Syriac about the twelfth century, but unfortunately the translator's name is also unknown, for the Syriac manuscript was mutilated, perhaps because it contained theories or statements which were not acceptable to monkish readers. We are told that "dysentery (or bloody disease of the inside) begins with evacuations of bile in large quantities which cause griping pains, and afterwards portions of the bowel come forth and then a little blood. These portions of the bowels must be carefully examined, for they indicate the place where the ulcer, which causes the dissolution of the bowel substance, is situated. When the ulcer is in the upper part it may be treated by medicines that are drunk, but when it is in the lower part astringent injections must be used. Ulceration of the bowels does not arise suddenly."

In another place the author says that the bloody diarrhœa "is like unto the water in which meat that hath just been killed hath been washed." There is a wealth of prescriptions, and one, containing 44 ingredients, is described as "a most

excellent and marvellous medicine, and no other existeth which is to be compared with it." After this high praise the practitioner must have been disappointed to read: "The dose is according to what God shall show thee."

In Europe, with the exception of plague, the epidemics in early days of which we hear most are typhus, malaria, and dysentery. The last named was certainly prevalent in France in A.D. 534, in Hungary in 820, in Germany in 1083 and 1113, and in England in 1316. Wars, famine, and foul drinking water were the chief allies of the various epidemics. The camp at Bordeaux, for instance, lost 14,000 men from dysentery in the year 1411 (Walsingham). Like malaria, dysentery reached its maximum diffusion and its greatest endemic severity in the tropics, while in subtropical countries there was, and still is, a decrease in the prevalence and seriousness of its endemic and epidemic incidence. Unlike malaria, epidemics of dysentery have attained northern latitudes such as Sweden and Iceland, though the disease has apparently found difficulty in prolonging its endemic existence in cold countries. King John is said to have died at Newark-on-Trent in 1216 from dysentery, aggravated from indulging too freely in peaches and copious draughts of new cider.[3] Edward I. is also said to have suffered from dysentery shortly before his death in 1307.

The earliest entries of dysentery which Creighton can find in the parish registers of England occur in 1596, when out of 28 burials during the year at Finchley 19 persons had died from dysentery, while in the following year there were 23 deaths from this cause out of a total of 48. Both these were years of scarcity all over England, and dysentery, with or without "famine fever," became the chief sickness in succession to declining plague.[4] In Stuart times dysentery began to be constantly heard of as a malady of London, called the flux or flix, and occurred in the bills of mortality after 1657 under the name "griping of the guts." The recipe for dysentery of the Hon. Robert Boyle (1627–1691), the most celebrated natural philosopher of his time and one of the founders of the Royal Society, was: Take the bone of the thigh of a

hanged man, calcine it to whiteness, and give the white powder in some red cordial. In addition to scurvy our sailors suffered severely from dysentery, and Sir Francis Drake in 1596 had to keep his cabin, complaining "of a scouring or flux," 13 days before he died off the Spanish Main.

In 1655 Cromwell's ambition to convert a Spanish island into an English colony led to many disasters. A naval and colonial force of 8000 men failed to take St. Domingo, chiefly because the troops (who had been revelling in oranges and other fruit and were therefore probably not scorbutic) "were troubled with violent fluxes, hundreds of our men having dropped down by the way, some sick, others dead." During the three weeks of this disastrous campaign on the island there were 1700 deaths, mostly due to "flux." The expeditionary force sailed on to Jamaica, where the Spaniards offered little opposition, but dysentery was almost universal among our officers and men. There was no care of the sick, no medical attention, no hospitals, no scavenging, no effort to protect the water-supply, not even energy to bury the dead. A despatch to Cromwell from his new possession stated that the army (which had meantime been reinforced) was reduced in January, 1656, to 3000 men, many of them sick and weak. "We die daily, not less than 50 every week, which is much, considering our small numbers." In this haphazard fashion did England become the owner of an island which is extolled to-day as a health resort!

The slave ships which transported negroes from Africa to North America were decimated by dysentery; the unfortunate slaves were beaten by the sailors, fed on salt beef and pork, and, to ensure cleanliness, they were forced into a tub of cold water every day, while a bucketful was poured upon their heads, in spite of their illness. Lettsom (1744–1815) practised as a young man in one of the West India Islands, where dysentery was certainly feared, and in consequence it became the custom of the residents to take their own drinking water with them when they were invited to dine on board a British ship. He seems to have regarded malaria and dysentery as twin associates and to have been certain that the latter was contagious. In 1772 he

wrote: "Every writer now allows the dysentery to be so, and the nature of this disease and remittents is so analogous that they seem to proceed from the same causes, somehow disposed to attack the body in a different manner; they even admit of mutual and alternate changes one with the other, and the method of cure in both is nearly the same, if we allow for the different symptoms liable to arise from the topical affection of the intestinal canal" ("Reflections on the General Treatment and Cure of Fevers," Section II.).

Records in British Isles.

In London, dysentery seems to have reached its chief prevalence in 1629, when the bills of mortality began to be regularly printed. In that year 449 deaths, being one-twentieth part of the mortality from all causes, were entered under the name of "bloody flux," while in succeeding years the heading was either "griping of the guts," which Creighton says also included infantile diarrhœa of the summer or autumn, or "surfeit," a term based on the erroneous theory that dysentery was caused by a surfeit of fruit. In the latter half of the seventeenth century Sydenham and Willis reported from London that there was a certain amount of dysentery every year, especially in camps and in prisons, but that it was not very contagious nor often mortal, except in the case of aged persons. But in 1689 there were two terrible outbreaks among troops at Londonderry and Dundalk. During the siege of Protestant Londonderry by the Catholic Irish army of James II., which only lasted 105 days, it was calculated that 10,000 (out of 30,000 besieged) died from fluxes, fever, and famine, "besides those who died soon after." Twenty-six days before the besiegers withdrew in consequence of the arrival of an English ship, some 500 useless persons were expelled by the garrison, and the besiegers are said to have recognised them when they met them "by the smell." A month later the released garrison carried dysentery and typhus to Schomberg's camp at Dundalk, where about 1700 died in spite of the routine treatment of casks of brandy, which were distributed among the regiments.

Story, a regimental chaplain, who wrote a history of this campaign, says that he found his own men in a state of brutal callousness, objecting to part with their dead comrades because they wanted the bodies to sit or lie on, or to keep off the cold wind!

Ten years before these two calamitous outbreaks Borlase had written, "The dysentery or flux is commonly called the country disease, and well it might, for it reigns nowhere so epidemically as it doth in Ireland." Sydenham was therefore justified in writing of the endemic dysentery of Ireland. When it ceased to be indigenous it became an occasional scourge, but since 1846–47 Ireland has apparently been free from epidemic dysentery. Graves (2nd ed., 1848) does not devote much space to this disease in his clinical lectures, but impresses upon his pupils the importance of putting patients suffering from chronic dysentery upon a "full meat diet." He possibly had famine or scurvy in his mind as a likely cause. Between 1759 and 1764 Dr. Mark Akenside in London treated at St. Thomas's Hospital 130 cases of dysentery, and proved the good effects of ipecacuanha upon many of them. He also pointed out that some of his autumnal cases did not abate until the following spring. But we cannot to-day accept his teaching that dysentery is "a rheumatism of the intestines."

At the end of the eighteenth century dysentery was easily transported from one country to another; for instance, transports conveying troops to Jamaica landed 400 sick with dysentery, though five months had elapsed since they left England. In much the same manner, and by what seems to have been a more usual process, imported cases infected our seaports. As an example, we read that the dock labourers of Newcastle were mortally infected in 1781 by dysenteric sailors who had returned from abroad.

Hirsch tells us that the first notice of a pandemic diffusion of dysentery over Europe dates from 1538, and that this was followed by at least six other similar pandemics, some of which lasted for three years or more. The last widespread European epidemic was in the years 1853–55, in France, Switzerland, Germany, Denmark, Sweden, and

Russia. Many parts of Scotland and England were attacked in 1846–47, and even in the twentieth century the disease has been more or less endemic in European Russia, Austria, Hungary, the Balkan States, Spain, and Italy. It is, therefore, somewhat premature to label acute dysentery as a tropical disease, though, so far as the British Isles are concerned, it may now be considered an exotic, with the exception of cases still met with in lunatic asylums, to which I must refer in the final lecture. Dysentery is indigenous in many parts of Asia, such as the Hejaz, India, Ceylon, China, and Japan; in Australasia it is well known in Queensland, British New Guinea, Fiji, and many other islands. In Africa and its islands the disease is a common one in most of the inhabited districts, and this is almost true of North, Central and South America, and the West Indian Islands.

Famines.—All through history it has been known that dysentery is an early attendant on long-continued famine, though it does not now exhibit a very infectious character when refugees introduce it. Yet the effect of the Indian famine of 1897 was to increase fourfold the deaths from dysentery and diarrhœa. In 1900, which was the last famine year in India, the deaths from bowel complaints rose from 252,025 to 530,654, being an increase of more than 111 per cent. The mortality in the Punjab and elsewhere was most marked in the famine districts. The failure of the rains in 1899 had led to the use of foul, stagnant, concentrated water from pools, while the rains of 1900 carried into the water channels an unusual accumulation of impurities; the people had to fill an empty void with indigestible food, such as badly cooked or raw grain, grass seeds, leaves, bark and roots, while after the onset of the rains they gorged themselves with green, fresh vegetables.[5] My own limited experience of famine-stricken Sudanese, imported into Egypt, compels me to admire the acumen of Herodotus, who attributed the dysentery which destroyed Xerxes' army, not so much to starvation as to the men having been obliged to try and support life by subsisting on the bark and leaves of trees.

Association with Wars.

Since the Peloponnesian war there has hardly been a protracted military campaign in which dysentery has not scourged the hostile armies. To take only some modern instances: in the American Civil war the Federal troops lost 37,794 men from dysentery and diarrhœa, which was nearly 30 per cent. of the total deaths; these diseases were also frightfully prevalent among the Federal prisoners at Andersonville, where they occasioned 50 per cent. of the sickness and 58·7 per cent. of the deaths from all causes. In the Franco-German war (1870–71) there were 38,652 admissions and 2380 deaths from dysentery in the German army; the troops on their return home spread infection in many districts, some of which, after all these years, are not yet quite free from it. In the South African campaign (1899–1902) we had 38,108 cases of dysentery with 1342 deaths. There were many predisposing causes, which tended to produce chronic irritability of the intestines and made the troops susceptible to infection, such as the youth and inexperience of our men, great variations in temperature, causing chills, extremely tough meat rations, and the very bad condition of the teeth of a large number of men towards the close of the campaign.

But the greatest source of danger which we encountered in South Africa was undoubtedly the water-supply. In standing camps, during the latter part of the war, all water was boiled; in hospitals and messes Berkefeld filters were used, but to carry out boiling properly large quantities of fuel are required, an almost insurmountable difficulty in a treeless country. On the march it was found practically impossible to prevent men from drinking foul water.

Great care was taken to select the best possible source; medical officers went on ahead of the column to select the place for filling the water carts. Sentries were posted to prevent animals and men, especially natives, from fouling the supply, and a European was placed in charge of the carts to see that they were filled at the selected spots. All this was well carried out in camp, and also when the

columns arrived on the camping ground sufficiently early, but frequently it was after dark, and possibly pouring with rain, when the carts were probably filled at the nearest place. Then, as fire and lights were not allowed if the enemy were in the vicinity, it was impossible to boil water, cook food, or dig latrines.

Towards the end of the summer water became scarce and the choice of camping grounds was more restricted ; consequently the same ground was repeatedly occupied and the surroundings became more contaminated. Diseased and exhausted animals invariably make for water, and not having strength left to extricate themselves from the mud lie down and die, so where the banks of the stream are steep the mortality is very great. The Modder River, in particular, was full of the carcasses of animals.[6]

When Ladysmith was besieged it was a town ripe for an epidemic, with three dangerous factors present: (1) a bad water-supply from the Klip River, already polluted by drainage from the town and from the Boer lines up-river; (2) a perfectly inadequate method of dealing with sewage; and (3) a soil previously polluted and infected. Valiant efforts were made to mend matters. Engineers from H.M.S. *Powerful* and some railway men constructed a condensing plant with locomotive boilers, but as fuel became scarce the supply had to be limited; rough filters were made, and as long as fuel lasted the water was boiled, and officers noted an apparent improvement in the health of the men so long as such methods could be used, but they could only be very partially adopted. It was only in the hospital at Intombe that a continuous system of filtering the water through Berkefeld filters could be kept up. During the 120 days of the siege there were 1280 cases of enteric fever with 360 deaths, and 1841 cases of dysentery with 105 deaths. The high death-rate was greatly due to the scarcity of milk and other suitable nourishment. The rations for the troops for the last six weeks of the siege consisted only of three small biscuits and $1\frac{1}{4}$ lb. of horse or mule flesh, or its equivalent.

The 48 medical officers who were in Ladysmith made gallant efforts, as the following record shows: 5 died, 10 had severe attacks of enteric fever, and 12 others were incapacitated, which shows what a strain must have been thrown upon those who could remain at their posts. On the

relief of Ladysmith there were 2000 sick and wounded in the hospitals and at least as many more who were only fit to be invalided. The relieving force, which had spent a fortnight in the horribly insanitary positions lately occupied by the Boers, at once added an enormous number of sick to the garrison. Sir Frederick Treves was among the first to enter the town with the relieving force, and this is what he says:—

> The men were piteous to see; they were thin and hollow-eyed, they had about them an air of utter lassitude and weariness. Some were greatly emaciated, nearly all were pale, nearly all were silent. They had exhausted every topic of conversation, it would seem, and were too feeble to discuss even their relief. Streets were empty of all but a few tired and listless men, stores without goods, shops without customers, a railway station without passengers, a post-office without letters, stamps, or postcards. No words, indeed, can fully describe this city of desolation, this little colony of the almost hopeless, this poor, battered, worn-out, hungry town of Ladysmith, with a bright summer sun making mockery of its dismal streets. The wretchedness of the place was not mitigated by the horrible smells which greeted one at every corner, nor by the miserable, dirty river which crawled slimily through the place.[7]

As a postscript of dysentery in South Africa I may add that an outbreak of 170 cases and 38 deaths occurred at Aldershot in 1901, apparently due to importation of the disease by returning troops.

Let us turn for a minute to Japan, where there was, during 1894, the enormous number of 155,140 cases of dysentery, of which 38,094 died.[8] From the sanitary point of view the Japanese had fared badly in their land campaign against China in that year, losing 3 from disease to every 1 wounded. But they took the lesson to heart and proceeded to mend matters, so that, when they fought and beat the Russians in 1904, instead of a proportion of 4 deaths from disease to 1 death from wounds, which Sir Thomas Longmore tells us is the average of the wars of the last 200 years, the Japanese reversed those figures, having a mortality of 1 dead from disease to 4 dead from wounds. Those British officers who were allowed to accompany the Japanese troops report that sickness was kept down by reliance upon every soldier carrying

out the regulations taught to him in peace time rather than upon any expert sanitary corps. Every Japanese soldier is taught that the most disgraceful illness to which he can succumb is one induced by disobedience to orders, such as drinking dirty water or eating unwholesome food. The national habit of drinking tea, which necessitates boiling the water, was of great preventive assistance. But when the Japanese was unable to boil the water he suffered just as others do. For instance, before Port Arthur there was an advanced post of 300 men, whose only water-supply came from a surface well which they had dug. The post was close to the Russian lines, so that fires for boiling water were not permitted. The water was good enough unboiled until, one day in August, a heavy storm of rain flooded the well and doubtless contaminated it. "The men drank the water as usual, and next morning they were nearly all down with dysentery."[9]

The mortality from dysentery among the Japanese was often as high as 25 per cent. of the cases, which can be explained by "the fact that 90 per cent. of the dysentery cases were complicated with beri-beri." In the recent war between Italy and Turkey in Tripoli, and again in the Balkan campaign, dysentery was present among the troops, but no complete statistics have yet been published. Dr. Stiven, however, who was near Constantinople in the war of 1912–13, caused to be examined in his hospital laboratory 228 specimens of fæces, with this percentage of results : cholera, 10·9 ; bacillary dysentery, 35; B. coli enteritis, 54·1 All the dysentery cases examined were of the Shiga type, and no cases of amœbic dysentery were detected. Many of the B. coli cases may have been originally bacillary cases of dysentery; others were due doubtless to starvation and exposure. "A spore-bearing bacillus was often detected on examining the fæces of patients. This was supposed to be the B. enteritidis sporogenes, and was identical with a spore-bearing bacillus found on maize and other roots. The old soldiers knew that if they ate these roots raw or insufficiently cooked they would get diarrhœa, but that it would yield to treatment."[10]

The so-called dysentery from which Sir Ernest

Shackleton's party suffered in the Antarctic zone seems to have been an irritative enteritis due to too rapid a return to meat diet. The usual ration on the march in Polar expeditions consists of dried pemmican (dried beef 23 per cent., marrow and oatmeal fat 63 per cent., water 14 per cent.), biscuit, cocoa or tea, butter and sugar, and Surgeon Atkinson, R.N., a member of the late Scott expedition, tells me that upon returning to camp, in spite of a consuming desire for food, it is better to limit the diet to porridge and bread, for even they produce some diarrhœa, and to withhold all meat for at least six days.

Dysentery slowly Admitted to be Water-borne.

Even after experts had hesitatingly accepted the belief that cholera and enteric fever epidemics were often caused by the impurity of drinking-water, they were unwilling, until the very end of the nineteenth century, to admit dysentery under the heading of "water-borne diseases." For instance, Fayrer (1881) quotes with apparent approval Fergusson, who wrote: "True dysentery is the offspring of heat and moisture, of moist cold in any shape after excessive heat, but nothing that a man could put into him would ever give him true dysentery." Again, in 1891, Notter,[11] while eliminating scurvy and malaria as possible factors, stated that there was little doubt of the correctness of Cullen's view that dysentery and diarrhœa were produced "from the effluvia of putrefying animal substances." It is true that he mentions that two observers in India had directed attention to impure water as an occasional cause. In 1895 Notter's late assistant published an excellent "Handbook of Hygiene," but did not include dysentery as one of the three important diseases caused by impure water, though he states "if dysenteric stools gain access to water it is most probable that such water, if used for drinking, would spread the disease, as in enteric fever and cholera. Proof of this is not, however, forthcoming at present."

I cannot quite remember when I first became

aware that dysentery should etiologically be grouped with cholera and enteric fever, but I recall with great distinctness an incident which occurred during the reoccupation of the Sudan shortly after 1895. An English regiment, during a forced march in hot weather near Dongola, exhausted their drinking water and, maddened by thirst, rushed to an obviously unclean pond which they came upon towards the end of the day. As a direct consequence some 150 soldiers of this regiment developed dysentery, while three weeks later 50 men from the same regiment were down with enteric fever. The officers believed that this one indiscretion caused 52 deaths.

Profiting again by the analogy of enteric fever, we now firmly hold the conviction that dysentery can also be conveyed to man by contaminated food, by flies, and by human carriers. Even now it is not universally recognised that dysentery, under certain circumstances, is communicable from man to man, and that isolation is as necessary in this disease as in enteric fever. The Japanese army includes enteric fever and dysentery among the infectious diseases which have to be isolated. Because malaria has so often in the past been thought to be a cause of dysentery, I should perhaps mention that, though the two diseases are frequently found to be coexisting, we do not now believe that either malady is the cause of the other, nor do we any longer think that drinking water from a marshy district can by itself produce malaria. There is, however, in warm countries a malarial enteritis which simulates true dysentery, and of this I am convinced, because I have twice suffered from it.

During the construction of the Panama Canal the Americans were confronted with the three local scourges—yellow fever, malaria, and dysentery. Their success in lowering the death-rate of dysentery, chiefly by improving the water-supply and by preventing flies from breeding, deserves to be mentioned here. The average dysentery mortality among canal employees during the French régime was 3·79 and under the Americans 0·60 per 1000; thus, though the number of workmen had increased sevenfold, the death-rate was more than

six times less than the average of the years 1881–1903. In the city of Panama the dysentery deaths fell from 8·93 in 1884 and 11·70 in 1902 to 0·51 in 1912, and even to 0·30 in 1911 per mille. During 1913 there were no deaths from dysentery among the 11,943 white employees and only six deaths among the 45,000 others.

Differentiation of the Two Types.

A good epitome of the evolution of our knowledge of dysentery before the differentiation of the two chief types, amœbic and bacillary, was given last year by Sir Leonard Rogers,[12] and I may now briefly refer to the separation of clinical dysentery into the two varieties amœbic and bacillary dysentery, for which we are indebted to microscopical and bacteriological research. In 1859, at Prague, Lambl first found living amœbæ in the fæces of a case of infantile diarrhœa, and in 1873 Lösch, at St. Petersburg, again found amœbæ in a case of chronic dysentery.[13] He injected fresh fæces containing these amœbæ into the rectums of four dogs, and produced in one of them dysenteric symptoms. Three weeks later this dog was killed, when dysenteric ulcers were found in the rectum, and amœbæ were present which Lösch named amœbæ coli. After looking at his drawings you will agree that his paper was well illustrated, but we now believe that he was dealing with what is to-day called Entamœba histolytica.

Other observers found amœbæ present in the motions of healthy people, so that these protozoa were still considered to be of doubtful etiological importance until Koch, in 1883, in Alexandria, and later in India, not only discovered the cholera vibrio but also amœbæ in sections of human intestines. He was then at the height of his fame and was a most stimulating teacher. Inspired by the enthusiasm which we all felt for him at that time, Kartulis investigated all the cases in his hospital in Alexandria, and eventually found amœbæ present in 500 dysenteric patients, while they were absent in other individuals. He also found amœbæ in sections of the intestines and in the pus and

walls of liver abscesses.[14] He defined two types of dysentery, that due to amœbæ, which he called "endemic," and another due to bacteria, which he suggested was "epidemic."

In 1890 Osler corroborated the discovery of Kartulis by finding amœbæ at Baltimore in a case of dysentery with abscess of the liver, which had originated in Panama. A series of similar cases in the wards of Johns Hopkins Hospital was then described by Councilman and Lafleur, who introduced the term "amœbic dysentery." In 1893 Kruse and Pasquale re-investigated the question in Egypt, and sought to solve the difficulty in the minds of many observers by suggesting that there were two species of amœbæ, one harmless and the other pathogenic. They also clinched the pathogenicity of the Egyptian amœbæ by producing dysenteric symptoms and lesions in cats by injecting into them, per rectum, amœbæ from dysenteric stools and from the pus of liver abscesses. Ten years later lingering doubts as to whether certain amœbæ were an etiological factor or not were removed by the publication of Schaudinn's paper on the life-history of human intestinal amœbæ, when he christened the harmless one Entamœba coli and the dysenteric one Entamœba histolytica.

In order to explain the etiology of the non-amœbic type of dysentery every few years since 1869 bacteriologists competed in the task of isolating a specific dysenteric bacterium from the very varied flora of the intestines. But it was not until 1898 that Shiga published his successful results of a study of epidemic dysentery in Japan. He had no lack of material at hand, for in 1897 there were 89,400 cases, with 22,300 deaths. In 36 cases which were investigated Shiga's dysentery bacillus was found either in the fæces or in the intestinal mucous membrane. He also proved that his bacillus agglutinated with the patient's blood under certain circumstances. In 1900 Flexner in Manila discovered Shiga's bacillus and also another differing slightly from it, which is now called Flexner's bacillus. Since then Kruse and many others in Europe have confirmed the existence of the two bacilli, while Strong and Musgrave had the

opportunity of proving by a crucial experiment the pathogenicity of the Manila variety. A Filipino prisoner under sentence of death agreed to swallow cultures of the bacillus. Characteristic symptoms of dysentery immediately appeared, the bacilli were obtained in culture from the stools, and then the man was fortunate enough to recover. Flexner tells us that one of his assistants accidentally aspirated into his mouth a small quantity of a culture of the dysentery bacillus; in spite of thorough and immediate disinfection of the mouth a sharp attack of dysentery followed, which ended, however, in recovery.[15]

Sceptics who maintained that amœbic dysentery was unknown in India and some other warm climates have now been converted, and the broad fact is well established that most of the dysentery of the tropics is amœbic, while much of the dysentery of temperate climates is bacillary. Bacilli are not, however, always absent from amœbic cases. For the last few years attention has been chiefly directed to the life-history of the amœbæ.

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LECTURE II.

AMŒBIC DYSENTERY.

THE physician must be able to tell the antecedents, know the present and foretell the future; must meditate these things, and have two special objects in view with regard to diseases, namely, to do good or to do no harm. The art consists in three things—the disease, the patient, and the physician. The physician is the servant of the art, and the patient must combat the disease along with the physician.—Hippocrates, "Epidemics," Book I.

THE ENTAMŒBÆ OF THE HUMAN INTESTINE.

This question is a complicated one, due partly to changes of nomenclature, and I therefore propose to devote a few minutes to placing on record the present position of our knowledge. In the preparation of this part of the lecture I have received much practical assistance from the well-known protozoologist, Dr. C. M. Wenyon.

As I stated in my first lecture, amœboid organisms in the human intestine were first satisfactorily described by Lösch in 1875. He gave the name Amœba coli to amœbæ which he had seen in the stools of a patient presenting dysenteric symptoms in St. Petersburg. From the figures and description given by Lösch it would appear that the organism observed by him is identical with the one which is now known to be the cause of amœbic dysentery. But for some reason which is not quite clear it is now generally assumed that he was dealing with the non-pathogenic entamœba of man, and in consequence the name Entamœba coli is now employed for this species. Many observers after Lösch recognised the possible pathogenicity of the human entamœbæ, and frequently demonstrated that dysenteric lesions could be produced in animals (cats, dogs, and monkeys) by the rectal injection of fæces from dysenteric patients.

In 1891 Councilman and Lafleur published a very exhaustive account of amœbic dysentery, and fully recognised its cause in an amœboid organism which they named Amœba dysenteriæ. There can be no doubt that these observers were dealing with the entamœba which is now recognised as the cause of amœbic dysentery throughout the world, and if we still adhere to the view that Lösch was observing the non-pathogenic form, then the name Entamœba dysenteriæ is the proper name for the common dysentery-causing entamœba of man. In 1895 Casagrandi and Barbagallo studied human entamœbæ, and gave a description (under Lösch's name Amœba coli) of the common non-pathogenic form, the one which is now recognised as Entamœba coli.

The Developmental Cycle.

Finally, Schaudinn came into the field and demonstrated clearly, what others before him had suspected, that the human intestine was liable to infection from two distinct organisms, one pathogenic and the other harmless, and that much of the confusion connected with the subject of amœbic dysentery was due to a failure to recognise this fact. Schaudinn re-described the Entamœba coli of Casagrandi and Barbagallo, who had previously recognised the encysted forms of Entamœba coli, and had fully appreciated their importance in the matter of survival outside the body of man and of conveyance of infection to a new host. They had observed that within the cyst the Entamœba coli multiplied, and that when the cyst came into a new host it ruptured and there emerged eight small, young entamœbæ which brought about infection. Schaudinn added little to this account except that he described a developmental process as taking place within the cyst, which was of the nature of a self-fertilisation, termed autogamy, and which preceded the division of the entamœba into eight daughter cells. This autogamy process for Entamœba coli has received no confirmation and many authorities even question its existence.

On the subject of the pathogenic entamœba Schaudinn confirmed much of the work which had

previously been done by others, and added further details relating to the developmental cycle. Unfortunately his researches were made on insufficient material containing degenerating entamœbæ, and they therefore cannot be regarded as correct. On the strength of his observations Schaudinn created for the pathogenic entamœba the name Entamœba histolytica, which is now generally employed. He described Entamœba histolytica as reproducing in the large intestine of man, by a simple division into two parts or by a process of gemmation whereby small buds having a diameter of 3–6 μ were separated from the parent organism. These buds were supposed either to grow into adult entamœbæ again or to become enclosed in very tough brown capsules, in which case they acted as spores, escaped from the intestine and brought about infection of a new individual. Hartmann has examined many of the preparations on which Schaudinn's account was based and finds that he was dealing with degenerating forms, which led him to deduce an erroneous cycle of development.

It is not to be wondered at that Schaudinn failed to recognise in his preparations the organism described by Councilman and Lafleur as Amœba dysenteriæ, for it had been studied in a far greater amount of material than Schaudinn had at his disposal. Councilman and Lafleur observed only the free amœboid forms and did not encounter the encysted forms which could convey the infection.

The next step in advance was made by Viereck (1907), who studied amœbic dysentery in West Africa and found that the organism producing the disease differed from that described by Schaudinn in that there occurred encysted forms which were very much like the encysted forms of Entamœba coli. They were, however, smaller, being 10–12 μ in diameter, instead of 15–20 μ, and led to the production of only four daughter entamœbæ within the cyst instead of eight. These encysted forms differed so much from Schaudinn's small brown spores that Viereck concluded that he was dealing with a distinct entamœba, which he called Entamœba tetragena.

Observers all over the world then began to look for Viereck's encysted forms (tetragena cysts), and

it soon became evident that wherever amœbic dysentery occurred, there the causative entamœba produced Viereck's cysts and never the small brown spores described by Schaudinn. The suspicion has since gradually gained ground, till at the present time it amounts to a conviction, that Schaudinn must have been wrong in his account and that the development described by Viereck, which led him to regard his entamœba as a new species, was simply the first true account of the development of the pathogenic entamœba of man, which had been studied by numerous observers in all parts of the world, and had been first named Amœba dysenteriæ by Councilman and Lafleur and, later, Entæmœba histolytica by Schaudinn. The true name for the pathogenic entamœba of man should therefore, by priority, be Entamœba dysenteriæ. It should, however, never be forgotten that Schaudinn was the first clearly to recognise two distinct human entamœbæ, one pathogenic and the other non-pathogenic, and that this did a great deal to clear up the existing confusion.

The Parts Played by the Two Forms of Amœbæ.

At the present time the most accepted view is that the large intestine of man is liable to infection by two distinct entamœbæ. One of these, Entamœba coli, is a harmless organism, living merely on the intestinal contents and never penetrating the mucous membrane. It reproduces by simple division, and possibly by a multiple segmentation into eight, also in the intestine, and occasionally becomes enclosed in transparent spherical cysts, having a diameter of 15–20 μ, and within which in the next host it ultimately divides into eight daughter entamœbæ. These cysts are passive bodies and escape from the intestine naturally with the fæces, and, being resistant, they protect the entamœbæ within till chance shall bring them into the intestine of a new host.

The second entamœba, the Entamœba dysenteriæ (E. histolytica, Schaudinn, or E. tetragena, Viereck), is a pathogenic organism which not only lives amongst the intestinal contents, but actually

invades the tissues of the large intestine, leading to all the troubles and symptoms associated with amœbic dysentery. This organism reproduces in the intestine by simple division like Entamœba coli, and also sometimes becomes encysted in transparent cysts having a diameter of 10–12 μ. Within the cyst there are produced in the next (human) hos four daughter entamœbæ, and, as in the case of Entamœba coli, the cysts are responsible for the carriage of infection from one individual to another. As the entamœbæ themselves survive only a short time outside the host, the importance of these encysted forms is evident, for it is by their agency that amœbic dysentery is kept going. While living in the intestine of cases of active dysentery the entamœbæ are large organisms 20–30 μ or more in diameter, and in this condition they invade the tissues and produce the extensive undermined ulcers so characteristic of the disease.

During the height of the dysenteric attack, when there is active invasion of the tissues, encysted forms are not produced, but as the dysenteric process abates, possibly by way of protecting themselves against antibodies, the entamœbæ begin to encyst. Prior to encystment, however, the characters of the entamœbæ change somewhat, and instead of comparatively large organisms there appear smaller forms having a diameter of only 10–20 μ. This small type differs also in the character of its cytoplasm, so much so that Elmassian, in 1909, was led to describe it as a distinct entamœba under the name of Entamœba minuta. It is now known that these represent the pre-encysting generation of the pathogenic entamœba. Persons who have apparently recovered from an attack of amœbic dysentery may have entamœbæ of the "minuta" type multiplying in the intestine apparently without there being any active invasion of the tissues.

During this time the entamœbæ are constantly encysting, and the individual may be passing, with a little mucus, enormous numbers of the infective encysted forms in the stools. Such individuals are termed by E. L. Walker and A. W. Sellards "convalescent carriers," and they are not only in a condition dangerous to themselves, in that

they are always liable to relapse, the "minuta" forms of the entamœbæ giving place to the large active tissue-invading forms ("histolytica" forms), which begin again their destruction of the wall of the large intestine; but they are exceedingly dangerous to other people, in that they may be distributing broadcast the infective cysts, which have only to gain entrance to the intestine, in the food or water, to bring about infection. Such individuals are, in fact, infinitely more dangerous than those who are suffering from acute dysentery and who are passing only the large non-infective "histolytica" forms. It is not known with certainty exactly how long such "convalescent carriers" may harbour the "minuta" forms of the pathogenic entamœba without themselves suffering a relapse of their old symptoms or ridding themselves of their infection. It may at least be for a period of several months.

Walker and Sellards have described, under the name of "contact carrier," another type of individual who is found to be infected with the "minuta" generation without ever having suffered from amœbic dysentery. They suppose that such persons have become infected by ingesting encysted forms, but that the entamœbæ, for some reason not understood, have not invaded the tissues and have remained in the cavity of the intestine as "minuta" forms, which reproduce there and encyst as in the "convalescent carriers." It may be concluded, therefore, that from the point of view of the already infected individual, the free entamœbæ are of importance because they are the tissue-invading forms, but that from the point of view of spread and dissemination of the disease the cysts only are to be feared. With a little experience it is easy to recognise and identify in fæces the encysted forms of either Entamœba coli or Entamœba dysenteriæ, but the identification of the free unencysted forms presents much greater difficulties, even to the expert.

Experimental Work.

It is impossible to enter here into the details of experimental work which has led to the view out lined in this lecture. It has been frequently shown that injection of the pathogenic entamœbæ into animals leads often to their infection and death from amœbic dysentery. Since the encysted stages of the entamœbæ have been recognised, more accurate experiments have been conducted. From the work of Darling, James, Wenyon, Walker, and others it has been shown that, in cats especially, the free forms of Entamœba coli injected per rectum and the encysted forms given per os do not lead to any dysenteric symptoms, whereas the free Entamœba dysenteriæ injected per rectum or the encysted forms given per os lead to intense infection of the large intestine, invasion of the tissues, and the production of a condition of affairs exactly comparable to that of a human being suffering from amœbic dysentery.

In a series of investigations undertaken at the London School of Tropical Medicine Wenyon carried on the infection in cats for a series of passages. The initial infection was produced by injecting per rectum and per os the stool of a patient who had previously had amœbic dysentery, but had recovered. It was found, on routine examination, that there was a large infection of the "minuta" form and numbers of cysts were being passed. In fact, the patient was a "convalescent carrier." The first cat so treated acquired typical acute amœbic dysentery, and there were passed thousands of entamœbæ which were large and of the "histolytica" type. No cysts, however, could be found. The gut contents of this cat, injected per rectum into a second cat, reproduced the condition of the first. A third cat was infected from the second and a fourth from the third. All the animals died of the disease and post mortem they all showed ulceration of the large intestine, which on section was found to be invaded by countless numbers of the large entamœbæ. The entamœbæ were also found in the mesenteric glands, while in the fourth cat there were found in addition four abscesses of the liver

containing numbers of large entamœbæ. In this cat there was thus reproduced not only the dysenteric condition of man but also liver abscess, which occurs as a complication in so large a percentage of cases of human amœbic dysentery.[1] The primary invasion of the intestinal wall by the entamœbæ can more easily be studied in the cat than in man on account of the possibility of obtaining material unaltered by post-mortem changes.

In the cat the entamœbæ enter the tubular glands of the large intestine and make their way to the deepest limits of these glands. Here they multiply and, by pressing on the cells and possibly by excreting some injurious toxic substance, they cause the cells to degenerate and separate. The entamœbæ then push their way between the cells and by means of their pseudopodia burrow in the submucous tissue. Bacteria are admitted and, together with the entamœbæ, bring about the tissue destruction so characteristic of the disease. The entamœbæ enter the blood-vessels, and it is probably by this route in the portal vessels that they reach the liver.

While producing experimental amœbic dysentery in cats by feeding them on material containing the "tetragena" cysts, Darling, in a similar manner, has been able to pass the infection from cat to cat. He has found that after a series of passages the entamœbæ tend to change from the "histolytica" type to the "minuta" type, and that there then appear in the fæces the "tetragena" cysts. He has therefore discovered in cats the same cycle of changes in the characters of the entamœbæ which occur in natural human infections.

Before leaving the subject of the intestinal entamœbæ of man reference must be made to some recent experiments carried out in the Philippine Islands by Walker and Sellards, who have shown conclusively by experiments conducted on men that the encysted forms of the two human entamœbæ are the infective agents, and that one is pathogenic and the other harmless. Of 20 men who ingested Entamœba coli 17 became infected, as proved by their stools, yet none developed the symptoms of dysentery. Of 20 men who ingested Entamœba histolytica (dysenteriæ), 17 became

infected after one feeding, while another became infected after three feedings. It was shown that ingestion of encysted forms only led to the appearance of mobile entamœbæ in the stools. In one case ingestion of cysts only led to the appearance of free entamœbæ and, later, encysted forms, and, still later, free entamœbæ again, an alternation repeated several times. Ingestion of free entamœbæ (after neutralisation of the stomach contents) led to the appearance of entamœbæ in the stool. Of the 18 men who became infected with the pathogenic form, 4 developed amœbic dysentery. The incubation periods up to the time of onset of symptoms in the 4 cases were 20, 95, 87, and 57 days respectively. It is interesting to note that these 4 cases were all infected from either "contact" or "convalescent" carriers. The disproportion between the number of men (18) who became infected with the pathogenic entamœbæ and the number of these (4) who actually developed dysentery is worthy of remark in showing how easy it is for an individual to become a "contact" carrier without actually acquiring dysentery itself.[2]

It must be mentioned that upwards of 20 different species of entamœba have been described from the human intestine by various observers. It may very safely be stated that none of these have been sufficiently studied to exclude the possibility of their being other than modified forms or involution forms of one of the two entamœbæ described above. It is true that occasionally amœboid organisms, resembling the free-living amœbæ of the Amœba limax type, are encountered in the intestine, but these must be clearly distinguished from the entamœbæ. They are probably free-living forms which have obtained accidental entrance to the intestine in an encysted condition, and, finding the contents congenial, for some reason or another, have proceeded to grow and multiply there, without in any sense being parasitic and dependent upon the host, as are the true entamœbæ.

Pathological Anatomy.

The primary lesion of amœbic dysentery is apparently an exudation into the submucous coat of the large intestine, first seen to the naked eye as red, slightly raised spots, not much larger than the head of a pin. When these congested spots grow in area a yellow central point appears, which is the earliest stage of ulceration, due to local necrosis of the mucous membrane. It is rare to see the early stages of ulceration, unless the patient has died from some other disease, but at the post-mortem examination of a case of acute dysentery it is sometimes possible to see all the various stages in the same intestine. The ulcers have a tendency to extend in a circular or ragged form around the bowel and are sharply limited to the large intestine. Another characteristic of amœbic dysentery is that the whole intestine is not uniformly affected, for there remain areas of quite healthy mucous membrane between the thickened and abruptly raised patches of ulceration. In a neglected case of severe amœbic dysentery the thickened intestine can be easily felt through thin abdominal walls. In gangrenous cases the ulceration extends to the serous coat and occasionally causes perforation of the lower bowel and peritonitis.

In at least half the dysenteric necropsies which I have performed or witnessed in Egypt and Turkey the whole of the large intestine has been attacked, with the exception of the heathy areas just mentioned, and in comparatively early cases the lesion was more advanced in the lowest part of the large intestine. Sir Leonard Rogers, after 12 years' experience of more than 100 dysenteric post-mortem examinations in Calcutta, finds that the ulcers are often limited to the upper parts of the large bowel the sigmoid and rectum remaining free.

I have the opportunity of showing you pathological specimens of dysentery from different parts of the world, mostly borrowed from the museum of the London School of Tropical Medicine. The following is Professor Symmers's post-mortem note of an Egyptian, aged 30, who died in 1903 in

the eighth week of dysentery, after the number of daily evacuations had been reduced from 14 to 4 by enemata of boracic acid and sulphate of copper.

CASE 1.—The whole of the large bowel from anus to ileo-cæcal valve showed numerous circular ulcers from $\frac{1}{4}$ to 1 inch in diameter, crateriform in appearance, with elevated and slightly undermined margins of a bright red colour. Most of these ulcers were covered by thick masses of yellowish matter, practically amounting to a false membrane. This dysenteric condition ceased with absolute abruptness at the very commencement of the small bowel, which was normal except for some slight prominence of the solitary lymph follicles.

Such a post-mortem appearance makes the physician despair of attempting any drug treatment, unless it is certainly amœba-cidal.

The microscopical appearances of early amœbic ulcers show a considerable small-celled infiltration of the submucosa, which elevates the mucous membrane to form the raised spots on the inner surface of the bowel. This infiltration consists of leucocytes and amœbæ, which latter have the power of burrowing between the muscular fibres, and so may reach the subserous coat. They may also penetrate the veins and enter the portal system, accounting eventually for inflammation or abscess of the liver.

Half a century ago dysentery used to be one of the chief diseases of Egypt, both among the natives and Europeans. The death-rate from that disease in the European hospital in Alexandria[3] was 16·7 per cent., while Griesinger at Kasr-el-Ainy Hospital in Cairo found 186 cases in 363 necropsies, of which he called 96 primary or idiopathic and 90 secondary. Dysentery is decidedly less common to-day, for the Kasr-el-Ainy statistics during the four years 1910–13 record that there were 11,108 in-patients in the medical wards, of whom 345 had dysentery and 53 of them died. To them we ought, perhaps, to add 233 other cases of bilharzial dysentery, because it is unlikely that they would have been differentiated in Griesinger's time. But after this addition the sum only amounts to 5·2 per cent. of the medical cases admitted to the chief hospital in Egypt.

Clinical Description.

Amœbiasis is a convenient name for specific lesions in various parts of the body, intestine, liver, brain, skin near anus, &c., and amœbic colitis has been proposed by Dr. Strong and Sir L. Rogers as a preferable term to amœbic dysentery, because it includes the sporadic mild cases, even when accompanied by constipation, in addition to those characterised by frequent evacuations and the constant presence of tenesmus, blood, and mucus. We now know that amœbic ulceration of the large intestine may continue for months unaccompanied by the classical signs of dysentery, and in such cases only careful and repeated examinations of the fæces will reveal the true nature of the disease. It is therefore important not to overlook this colitis in its latent phase.

The existence of tenesmus, often the symptom forcing the patient to seek medical aid, means that there are lesions in the proximity of the sphincter. If the lesions, on the contrary, either in true dysentery or in bilharzial infection, are limited to the colon, there will be no tenesmus. It is not rare to find a patient in this country who has recently returned from the tropics and is complaining of slight indigestion, constipation, and vague pains in the intestines. On palpation it may be found that there is tenderness over the colon but none over the small intestine. A dose of sulphate of magnesia, followed by a careful microscopical examination of fresh warm fæces by an expert, may reveal the presence of Entamœba histolytica and ensure the correct diagnosis of the malady.

The following case shows that one negative examination by the microscopist, especially in a cool laboratory, must not preclude the possibility of the presence of amœbæ :—

Case 2.—In 1897 a thin Egyptian, aged 35 years, was transferred from the eye wards to my care in Cairo. Clinically, there was no doubt about the dysentery, and he passed, in the first 24 hours after transference, 27 typical motions. Yet Dr. Ruffer, who personally examined the stools on that day, reported "plenty of pus, no amœbæ."

Two days later, when there were 10 motions, he reported "blood-stained liquid stool, containing no fæcal matter, but large quantities of slimy shreds, some of them blood-stained. Microscopically, a few red blood corpuscles and an enormous number of rather small amœbæ with clear protoplasm and vesicular nucleus. Temperature of room 60° F. (Jan. 16th). Amœbæ non-motile at that temperature

The next day the report stated that amœbæ were present in fairly large numbers, and the fæces were still shreddy and slimy. On Jan. 18th, when the number of daily motions was reduced to eight, the stools were " not fœtid, fluid, with shreds of mucus, some slightly blood-stained. Pure culture of granular amœbæ, nucleus small without nucleoli, protoplasm granular, no movements. Temperature of room 60°." After Jan. 20th he never had more than one or two motions in the 24 hours, and began to put on weight. He was treated throughout, and apparently cured, by large doses of bismuth with tannic acid and opium in small quantities, and this may have been aided by large daily enemata of boracic acid and starch, in which I was then a believer.

The onset of amœbic dysentery is usually sudden and always begins with diarrhœa. Fever is not a marked feature, and when present is never high, so that I agree with the Panama experience that a temperature much above 101° F. usually betokens some complication.[4] The stools vary from day to day in number and in quality and, as I have said, in the presence of amœbæ. No naked-eye examination of fæces can be trusted to determine whether the patient is suffering from amœbic or bacillary dysentery, but I have learnt, partly from experienced hospital sisters, that a shrewd guess can often be made in this direction. For instance, if the mucus is of a deep red blood colour and purulent, not unlike the contents of a liver abscess, it is safe to prophesy that amœbæ will be found. It is impossible to tell by the pain or by the appearance of the patient whether a case is amœbic or bacillary. The pain is intestinal, and is specially great before and during an evacuation. A higher degree of leucocytosis, tenderness over the colon, and thickening of the large intestine are all in favour of the amœbic type. Mild cases, unrecognised as dysentery,

or untreated by emetine or ipecacuanha, are those which are liable to develop hepatitis as a complication, or to become chronic, lasting several months, or even a year, and producing anæmia and emaciation. Fayrer tells of cases in his own practice where Europeans had suffered from relapses of dysentery for 10 or 12 years.

The cause of death in amœbic colitis is generally perforation and peritonitis, succeeding ulceration of the colon or appendix. The most frequent complication is abscess of the liver, and I have seen in Egypt two cases of abscess of the spleen.

Importance of Washing Stools.

Dr. Edward Goodeve (1816–1880), when professor of medicine in Calcutta, used to teach the necessity of watching the stools by carefully washing them and allowing the different parts to separate, so that sloughs and mucus can be distinguished from fæces. "The state of the bowel, the stage of the disease, and the nature of the morbid process may thus be ascertained with much accuracy" (Fayrer, p. 38). Unfortunately, Goodeve never published his observations on dysentery, and this may possibly account for the fact that fæces would seem not to be universally washed when a case of dysentery (or ulcerative colitis) is being treated. I gather that this is not part of the training of a British hospital, for I have seldom found a nurse or a young doctor in or out of hospital who had ever washed a specimen of fæces to look for mucus or worms. I should therefore like to take this opportunity of reiterating the importance of washing dysenteric stools under a tap of cold water, rejecting the top liquid after a minute's delay, and thus continuing the process patiently and slowly until all trace of fæces has disappeared. The mucus or slough which remains, or the whole motion if desired, can be conveniently kept for the doctor's inspection in a large glass Petri dish, as invariably used at the Albert Dock Hospital.

In acute dysentery the earliest evacuations almost completely remove fæculent matter, but not fæculent colouring. The washed stools then

consist of rose-coloured mucus of gelatinous consistence. Such may be seen in private practice where the patient summons medical aid within a few hours, but in hospital cases the symptoms have usually been neglected for some days previous to admission.

In a neglected case sloughs are generally passed on the sixth or seventh day. These vary in size up to that of a man's hand. In fair constitutions these sloughs often have much the appearance and consistence of a preserved oyster. They are oval and nearly a sixth of an inch in thickness. They are made up of the whole depth of the mucous membrane, frequently backed with some of the muscular coat, the submucous tissue being largely infiltrated with the products of inflammation.[5]

It is only by washing the stools and inspecting them daily that one can accurately judge how the patient is progressing, and whether it is safe to increase the diet. We are also enabled to see whether the patient has been taking any forbidden article; an English patient on liquid diet once asked me if he might suck some oranges, and two days later I found that his washed stools consisted only of orange pulp which he had swallowed.

Diagnosis of Amœbic Dysentery.

In the fourteenth century John Arderne wrote in London of the importance of a differential diagnosis between dysentery, hæmorrhoids, and cancer of the rectum, while his contemporary, John Mirfield, knew that dysenteric symptoms were not all due to the same cause. Five centuries later we learned that the differentiation between amœbic and bacillary dysentery, as also the distinction between true dysentery and diseases of the great intestine, such as cancer or the infiltration of Schistosomum hæmatobium, can only be made with accuracy when Entamœba histolytica has been searched for under the microscope. When amœbæ are found in fresh, warm stools, without contamination by urine, or when a fragment of mucus is placed on a warm slide, a pseudopodium may be seen to be protruding a new process, which makes it certain that you are not

dealing with an epithelial or pus cell, or an air bubble or fat globule, or starch or proteid grains. If in a suspicious case amœbæ cannot be discovered, it may be worth while to pass a catheter into the rectum in order to examine the mucus which may become entangled in the eye of the instrument.

Rogers has rightly pointed out [6] that we are now furnished with an important practical help towards diagnosis by the discovery of the rapid curative action of emetine, because so far as we know at present this drug is only specific for amœbic dysentery. If the stools have not improved in number and character at the end of three days it is practically certain that the case in question is not one of pure amœbic dysentery. When in doubt as to the cause emetine may therefore be given as an aid to diagnosis, just as quinine has been used for many years to determine whether a fever is malarial or not. In Ceylon it is believed that many of the cases returned as dysentery in hospitals and dispensaries are really victims of ankylostomiasis. But the presence of the eggs of entozoa in the fæces should not preclude the possibility of a superinduced true dysentery, which may be amœbic or bacillary. Dr. Day lately informed me in Cairo that he had seen latent cases of bilharziasis of the rectum which became dysenteric when the host was invaded by amœbæ or bacilli; the rectal symptoms then yielded only to emetine or serum.

Lastly, it must not be forgotten that a patient may be suffering at the same time from the two chief types of dysentery. For instance, the returning pilgrims at El Tor, during the season 1910–11, showed a mixed infection of 90 cases out of a total of 328 dysentery admissions to the hospital. Rogers has recently analysed the most frequent errors of diagnosis in 1000 post-mortem examinations of medical patients in Calcutta.[7] He finds that the clinical diagnosis of amœbic dysentery has been misnamed tubercular or simple diarrhœa or peritonitis, while there have been single cases which were thought to be the following: Tubercular peritonitis, hepatitis, gangrene of rectum, intestinal obstruction, broncho-pneumonia, malaria fever, and anæmia.

Treatment.

There is an old superstition that nature ordains that an antidote to the ills of man shall be provided in close proximity to the source of evil. Those of us who in tender years learned this comforting doctrine from the nurses who pointed out the dock leaves growing not far from the stinging nettle may accept without surprise the fact that tropical South America provides for us Peruvian bark and Brazilian ipecacuanha, genera of the Rubiaceæ, and our chief armament in combating the two most widely spread tropical diseases, malaria, and amœbic dysentery.

Ipecacuanha.

Ipecacuanha is the root of Psychotria ipecacuanha, a small plant found in most parts of Brazil; this is known as Brazilian or Rio ipecacuanha, and is the only kind official in the British Pharmacopœia. Another variety imported from Colombia is known as Cartagena ipecacuanha; this is not official, though the United States Pharmacopœia admits both varieties. The term "ipecacuanha," derived from the language of the aborigines of Brazil, has been applied to a great number of emetic roots of South American origin. In an account of Brazil written by a Portuguese friar and published by Purchas in 1625 mention is made of three remedies for bloody flux, one of which is called igpecaya. In their work on the natural history of Brazil published at Amsterdam in 1648 Piso and Marcgraf described two plants to which the name was applied; one of these is now known to be the genuine ipecacuanha. The drug was in common use in Brazil at this time, but was not brought to Europe until 1672, when a traveller brought a quantity of the root to Paris. In 1680 a Parisian merchant became possessed of 150 lb. of the drug; it was largely prescribed by Helvetius, a Dutch physician practising in Paris, who kept its nature secret. The fame of the cures reaching the French Court, King Louis XIV. caused trials to be made, and as these were successful he

accorded to Helvetius the sole right to sell the remedy. In 1688 the French Government purchased the secret from Helvetius for £800, and made the nature of the remedy public. The botanical source of ipecacuanha was not finally settled until 1800, when Dr. Gomez of the Portuguese Navy brought authentic specimens to Lisbon. As the remedy increased in demand numerous substitutes resembling the true drug came into use; in 1872 Professor Balfour enumerated 15 emetic roots used in various parts of the world and agreeing, to a certain extent, in being more or less annulated or striated externally. The destructive methods of collection employed in Brazil and the slow growth of the plant were responsible for a considerable scarcity of the drug, and numerous attempts have been made to cultivate ipecacuanha in India, Ceylon, and other tropical countries; a considerable quantity of a good quality of the drug is now exported from Singapore.

Supersession and Reintroduction of Ipecacuanha.

As an expectorant and emetic ipecacuanha held its own in Europe and India, but it soon ceased to be regarded as a specific for dysentery and was superseded for years by calomel and opium. In 1858, Surgeon-Major E. S. Docker again introduced large doses of ipecacuanha (20–90 grains) after opium, and only lost 1 out of 50 cases among British troops in Mauritius. As the consequence of its reintroduction into India the death-rate from dysentery in Madras fell from 71 to 13·5 per 1000, while in Bengal it was reduced from 88·2 to 28·8 per 1000. Fayrer states that nearly 11 per cent. of the cases among British soldiers used to be fatal, yet Docker had to wait until 1880 before he received any recognition of the important services he had rendered to mankind, when a gratuity of £400 was given him.[8] His treatment was found vastly more useful than the previous methods of bleeding, blisters, and mercury.

Forty years ago we were taught by Murchison that all cases of dysentery should be treated by one or two doses of ipecacuanha with an initial dose of

laudanum and the application of a mustard leaf to the epigastrium, but when I was confronted with dysentery in Servia, Turkey, Egypt, and South Africa I failed to find that this remedy was a universal cure, and for some years almost entirely abandoned the use of ipecacuanha, putting my faith in the saline treatment, or in bismuth, tannigen, and tannic acid, with large enemata of nitrate of silver, sulphate of copper, or quinine.

I think it is now obvious that my failures, which were also experienced by many good clinicians in India and other tropical countries, were chiefly due to two facts: (1) we knew but little of the various types of dysentery, and when we met with no success or with very partial success we blamed the ipecacuanha, instead of discovering that we were very often aiming at bacilli with a weapon which we now know is only warranted to kill amœbæ; (2) we were taught to administer ipecacuanha in single doses, repeating it if it was vomited by the patient, and occasionally giving a third dose if necessary, but it was not the fashion to prolong the use of the drug. It hardly occurred to us to imagine that if slight temporary benefit occurred after one nauseous bolus, a permanent cure might be attained by continuing the remedy. Perhaps we should have been more persistent in our trials if we had had more faith in the wholly empirical remedy. The utmost that ardent supporters of the drug could tell us was that it was supposed to act on the liver and that extra bile was perhaps poured out to kill the unknown organism of dysentery and heal its ravages.

Thus ipecacuanha was again temporarily shelved in many dysentery countries until the use of it was revived by Sir P. Manson. When I first had the opportunity of seeing him prescribe it for amœbic cases by his own prolonged method, a dozen years ago, I confess to having felt very sceptical about its value. But I was at once impressed by observing that the house physicians, assistants, and nurses were all firm believers in the method and preferred it to other lines of treatment. Gradually, as amœbæ came more and more to the etiological front the scales fell from my eyes and I adopted the well-thought-out course of administration.

The patient is starved for four hours, say from 5 P.M.; at 8.45 P.M. a mustard plaster is applied to the epigastrium, the pillows are removed from beneath the patient's head, and 15 minims of laudanum in water are given to him. At 9 P.M. he has one dose of 30 grains of ipecacuanha, and to prevent vomiting he is kept absolutely at rest, the nurse being ordered to wipe his lips to prevent his even swallowing saliva for at least three hours, when he is allowed a small drink. The next night, with similar precautions, he is given 25 grains of the drug, preceded by 10 drops of laudanum. On the third night he takes 20 grains after 5 drops of laudanum. After this opium is no longer required and the ipecacuanha is gradually reduced to 5 grains and kept there till the course has lasted a fortnight, when the patient will have taken altogether 145 grains. The patients submit willingly to possible vomiting and rigid rest and make up by day for rather sleepless nights. The only improvement I have added to this method is that I give the drug in five-grain membroids or stearin-coated pills, which prevent absorption in the stomach.[9] Care must be taken that the capsules are not too well coated, for I once found an undigested membroid in the patient's fæces.

The Alkaloids of Ipecacuanha.

Pelletier in 1817 separated from ipecacuanha what he regarded as the emetic principle; this was named emetine.[10] His examination of the various American emetic roots in commerce showed important variations in their alkaloidal content. In 1894 and 1895 Dr. B. H. Paul and Mr. A. J. Cownley showed conclusively that the substance hitherto known as emetine was a mixture of several distinct bases; for one of these bases, itself uncrystallisable, but forming crystallisable salts, they retained the name emetine; the second base, which also formed crystallisable salts, they named cephaëline (the ipecacuanha plant was then known as Cephaëlis ipecacuanha). Traces of a third alkaloid were found, and this was afterwards named psychotrine.

The many varieties and substitutes for ipecacuanha were factors in themselves sufficient to militate against its successful use in dysentery; a further disadvantage was the emetic and depressant action of large doses. In 1890 Surgeon-Major Harris, of Simla, pointed out in a letter to THE LANCET[11] that de-emetinised ipecacuanha—meaning ipecacuanha freed from all its alkaloids—answered as well as ordinary ipecacuanha in the treatment of dysentery. Other investigators were unable to confirm this, and Bird showed in 1893 that some specimens of so-called ipecacuanha sine emetine contained up to 1·2 per cent. of alkaloid, whilst in other specimens the therapeutic value seemed proportional to the amount of alcohol-soluble extractive present, alkaloids being absent. Bird, and later Paul and Cownley, put in hand an examination of the non-alkaloidal extractive. It was found to have no emetic action in doses of 4–5 grains, but positive indications of any therapeutic activity appear not to have been obtained. Recently Finnemore has taken up the subject, but the results of any pharmacological investigations have not yet been recorded.

Official ipecacuanha root of good quality contains 2–3 per cent. of total alkaloids, of which emetine constitutes about 72 per cent., cephaëline 26 per cent., and psychotrine 2 per cent. In Cartagena ipecacuanha the emetine amounts only to about 40 per cent. of the total alkaloid, whilst the cephaëline reaches as much as 57 per cent. On account of the different proportion of the respective alkaloids, Cartagena ipecacuanha is excluded from the British Pharmacopœia. Of the two principal alkaloids cephaëline is regarded as the more active emetic but the less active expectorant. Chemically emetine is methyl-cephaëline, $C_{29}H_{40}O_4N_2$; Carr and Pyman have recently shown that psychotrine can be converted into cephaëline by reduction; a chemical relation between the three alkaloids is therefore established.[12] Several crystalline salts of the three alkaloids have been prepared and characterised.

Treatment by Emetine.

The use of ipecacuanha in dysentery was placed upon a scientific foundation by the observation of Vedder in 1910 that solutions of emetine, 1 in 100,000, have the power of destroying amœbæ of the A. limax type in broth culture.[13] Rogers confirmed this effect of emetine hydrochloride on Entamœba histolytica in dysenteric stools.

So early as 1829 emetine was employed with good effect by Bardsley, and again in 1890 Lieutenant-Colonel J. H. T. Walsh[14] administered it in dysentery with marked success. To Sir Leonard Rogers[6] our gratitude is due for his introduction of treatment by what is usually called the intramuscular, or, more accurately, the intracellular method. Like quinine the dose should *not* be administered immediately under the skin, for by this method, as usually recommended, painful lumps and bruises may occur. It is not necessary to insert the needle into the body of a muscle. The hydrochloride of emetine in sterile water is the most practical to use, and it may be injected three inches under the clavicle or elsewhere. I have never met with nausea or any other inconvenience except that there is very slight tenderness at the site on the day following the injection, and a few women have complained of slight muscular pain after a fortnight's course. An ordinary case requires half a grain of the salt morning and evening on the first day, after which the dose may soon be reduced to half a grain once a day; the reduction of the dose must be decided by the improvement in the patient and the stools. As no one yet knows for how long the treatment should be continued, and as I have seen several cases in London which had previously undergone a three days' treatment (without bismuth) in India, I have provisionally formed for myself the habit of giving daily injections for a week, and then injections on alternate days for a second week, and so far I have not met with any case which has relapsed after such dosage. By this routine method an ordinary case would get altogether about 6 grains, equivalent to 540 grains of ipecacuanha. In a gangrenous or critical case I

should not hesitate to give ½-grain, or even 1-grain, doses every four hours, if necessary. Emetine, when keratin-coated, may be given by the mouth at bedtime, but is liable to cause vomiting unless the ipecacuanha precautions are observed; it is not so rapid in its action as by the intracellular method.

As I have as yet had no experience of treating children with emetine, I may draw attention to two cases reported by Captain R. G. Archibald[15] from Khartum. One English girl, aged 2½, passing 23 motions in the 24 hours, received injections of ⅛ grain, which, spread over three weeks, amounted to a total of 2⅙ grains. Her sister, aged 8 months, passing six motions, only required four doses, each of 1/12th grain, to get rid of all entamœbæ and symptoms. It is probable that children, as with ipecacuanha, will be found to be very tolerant of emetine. Captain Archibald, probably very wisely, recommends that emetine should be continually administered once a week or once a fortnight for a period of at least three months after the apparent cure of the patient.

When all symptoms have yielded to emetine and yet cysts reappear from time to time in the fæces, it is possible that ipecacuanha by mouth may succeed in banishing them more easily than a return to emetine injections. In support of this suggestion I may mention that a medical man from India consulted me lately about himself. He had undergone emetine treatment for dysentery in India, and had no symptoms except that he voided a little mucus, which contained hundreds of the so-called "minuta" cysts. He then injected himself every two or three days for two months with ½ grain of emetine. The cysts persisted, but disappeared after ipecacuanha treatment by mouth.

Rogers has published some experiments carried out to determine the fatal dose of emetine hydrochloride; rabbits and monkeys were used, and, if we are to assume that man would be proportionately affected, he finds that the lethal dose for a man weighing 11 stones would be 15 grains intracellularly or 5 grains intravenously.[16]

There has been so great a demand for emetine during the last two years that its price has more

than doubled, and in consequence a cheaper alternative has been put on the market, called "amebetine," which consists of the three known alkaloids of ipecacuanha unseparated from each other. I have tried it in a few mild cases with good results and without causing vomiting.

Emetine would seem not to have a cumulative effect in the system, for a medical man who had contracted dysentery abroad, and who consulted me last year, was so pleased with the effect of the drug on himself that he continued intracellular injections, each of ½ grain, every night for three weeks, and then every other night for another three weeks, which makes more than 15 grains altogether. His last six injections were of amebetine. On coming to tell me of this protracted treatment, he said that he had never noticed nausea or any other discomfort. His appetite had steadily improved, his motions became of a darker brown colour, but still sometimes contained a little mucus.

Whether we employ emetine or amebetine, or whether any better derivative of ipecacuanha can be discovered in the future, we seem to-day to possess a chemical agent which can eventually destroy pathogenic amœbæ, not only in the laboratory, but also in the tissues and fluids of the living body. After 240 years of empirical use of ipecacuanha we can now dignify this drug as being parasitotropic for amœbic dysentery, and, what is better still, as monotropic, in Ehrlich's language—i.e., possessing a specific affinity for the protoplasm of the offending amœbæ, and yet being inert with respect to all the other constituents of the normal body.

During my recent visit to Ceylon I met an intelligent young English planter without medical training. He told me that he used to lose from dysentery about 40 imported Indian coolies every year in the labour force of 600 on his tea estate. He heard of emetine in 1913 and sent for some. He then treated all his cases of dysentery with the new drug, and during the following six months which comprised the dysenteric season he never lost a case. Dysentery is rife in all parts of Ceylon, and in 1911–12, 4576 cases were treated in the various Government hospitals, with 1665 deaths.

One-fifth of the cases were treated in the Colombo hospital among vagrants and those whose drinking water comes from shallow unprotected wells. In the planting districts the disease is associated with an indifferent water-supply, but many patients under treatment for dysentery are really suffering from ankylostomiasis. Dysentery and diarrhœa are also the commonest diseases among Ceylon prisoners, for in the same year 2445 cases, with 125 deaths, were treated in the jail hospitals, including 758 cases, with 57 deaths, in Colombo.

Notes of Cases.

Many cases which come to us in private or at the hospital have, of course, been treated with all care and skill. Others have had no such fortune, and I should like to give the notes of a case to show how dysentery ought *not* to be treated, always remembering that the patient's own history of his case may not be strictly accurate.

Case 3.—The patient, aged 27, an English baggage steward, was admitted into the Albert Dock Hospital in 1907. He stated that his dysentery had begun on leaving Penang for London, with 25 motions a day, blood, mucus, and tenesmus. He was immediately treated by the ship's doctor, who gave him a powder three times a day and a white mixture, followed by opium pills. During this voyage he was not kept in bed and was given ordinary food, and no ipecacuanha. On arrival in London he was still very ill and had 10 motions daily. He was then treated at his home in the country by a doctor for three weeks, who told him that no special diet was needed, but gave him a mixture and apparently thought lightly of the case, for he never inspected the fæces, though all details of the history had been supplied to him. The patient then left this doctor and dieted himself on light food, resting a great deal, though not actually in bed all day. This improved him so much that he went to sea again, though he still had three dysenteric stools daily. On the voyage out the ship's doctor gave him a mixture and powders, but never saw his stools nor prescribed rest nor special diet. When he reached Bombay he was much worse and had to be transhipped home. He thus came under a fourth doctor, who did his best to diet him but did not keep him in bed and never examined his fæces. On his return to London he had 18 stools per day and was sent to the hospital, where he was put to bed on a diet of milk

and barley water. He was then given the ordinary routine ipecacuanha treatment, with the result that after the first day the myriads of amœbæ were reduced to a few and after the third day none could be found. Tenderness over the colon and tenesmus disappeared, and he said he felt better than he had for months. On the third day in hospital he had only one stool, and this continued until he left the hospital, without blood or mucus and having increased in weight.

I am grieved to say that some ships' surgeons are to-day not supplied with emetine, which seems to me criminal carelessness.

I began to substitute emetine for ipecacuanha in the autumn of 1912, and have used it since in every case in which amœbæ could be found, and in a few others where none could be discovered. With the exception of Case 12, I have met with universal success. I will not lengthen this paper by detailing every instance, but I will give very briefly the account of six consecutive cases of amœbic dysentery treated at the hospital in the summer of 1913.

Case 4.—The patient, a Goanese, aged 38, contracted dysentery in Baltimore four months before admission. His five typical stools per day contained Entamœba histolytica and cysts. He was given eight injections of hydrochloride of emetine gr. $\frac{1}{4}$, followed by four injections of gr. $\frac{1}{3}$. No amœbæ were found after the fifth day of treatment, and the motions were reduced to three and after the sixth day to one per diem.

Case 5.—The patient, aged 37, a Lascar, had had incessant diarrhœa for two weeks, 12 typical stools daily containing amœbæ. I gave him five daily injections of amebetine gr. $\frac{1}{3}$, which reduced the number of motions to six, and the amœbæ could not be found on the second and succeeding days. The drug was stopped for three days, because he had an intercurrent attack of broncho-pneumonia; then he was given santonin to expel his round worms, and then he returned to amebetine, of which he had eight more daily injections of gr. $\frac{1}{3}$. This reduced the number of evacuations to one daily.

Case 6.—The patient, aged 27, an Englishman, from the tropics, gave a history of seven weeks' "diarrhœa." and had never been treated for dysentery. His motions contained amœbæ, mucus, and sometimes blood; they were watery and three or four in number per day. He had 15 daily injections of emetine gr. $\frac{1}{3}$, but from the fourth day of his stay in hospital amœbæ disappeared and he had a tendency to constipation.

CASE 7.—The patient, aged 46, an Englishman, had in Southern India three attacks of dysentery between 1907 and 1913, for one of which he was treated with ipecacuanha. On admission he complained of a dragging pain above the umbilicus, where there was slight tenderness on pressure and mucus in fæces, but there was no blood and the bowels only acted once a day. Amœbic cysts were found and he was at once put upon injections of emetine gr. $\frac{1}{3}$, which were continued for 12 days. There was no trace of intestinal tenderness or amœbæ after the sixth day, but mucus occasionally appeared in the fæces for two months. Before he returned to India he was given amebetine gr. $\frac{1}{2}$ every night for a week, because his liver was slightly enlarged and tender on deep inspiration. He gained $8\frac{1}{4}$ lb. in weight and stated that he felt quite well for the first time for $6\frac{1}{2}$ years.

CASE 8.—The patient, a Japanese, aged 47, infected probably at Penang or Yokohama, had had four weeks' "diarrhœa" before admission with abdominal pain. There were 12 stools a day, consisting of almost pure blood and mucus, while the microscope revealed amœbæ free and encysted, with ova of Heterophyes heterophyes. Emetine gr. $\frac{1}{3}$ increased to gr. $\frac{1}{2}$ daily, until gr. 8 had been given, reduced his motions from 12 to 2 daily and they became normal in appearance. He was in hospital for 25 days and voided after treatment 50 adult heterophyes worms.

CASE 9.—The patient, aged 31, an Englishman, was attacked by dysentery and treated with ipecacuanha 11 years ago, but has spent the last seven years in England, occasionally having slight reminders of the disease. On admission he was found to have daily six stools, which were dark brown, watery, and offensive, and contained mucus, but no blood. Amœbæ in large numbers, free and encysted, were seen. The amœbæ disappeared on the fifth day of emetine injections, and there was only one daily evacuation.

During the same months cases which were clinically dysentery, but in whose fæces amœbæ could not be found by repeated examinations, were also treated with apparent success by emetine. I give two typical cases of this series which were not complicated, as coloured patients so often are, by the presence of entozoa.

CASE 10.—The patient, aged 28, an Englishman, suffered eight years before from dysentery, and had a return of it 11 weeks ago, after leaving Australia, and rapidly lost 14 lb. weight. He had on admission seven motions a day, watery with undigested food, mucus, and blood, but no amœbæ

could be found. After nine injections of emetine gr. $\frac{1}{4}$, he had only one motion a day, formed and without blood or mucus.

CASE 11.—The patient, aged 25, an Englishman, had suffered from dysentery three years since and one year ago, but has been in England for the last 18 months. He had never been treated with ipecacuanha. On admission he had 12 motions daily, dark brown, offensive, watery with undigested food and mucus, but no blood and no amœbæ. During eight injections of emetine gr $\frac{1}{2}$, his motions became constipated and without mucus.

Among private patients I have treated a dozen cases, mostly from India, in whose fæces Dr. G. C. Low had discovered amœbæ, besides an equal number seen in consultation. Two of them were ladies who were suffering from habitual constipation. They all became apparently well after a course of emetine, the amœbæ vanished, and in none of them have I been able to hear of any relapse. One case was complicated by appendicitis, and an operation had to be performed directly the course of emetine was over. All patients state that after emetine treatment they have lost, among other things, an indefinite feeling of discomfort in the abdomen, which they find it difficult to describe.

In order to show that emetine is not universally successful in saving the lives of amœbic dysentery patients, I take this opportunity of reporting my one fatal case after 18 months' experience of the drug. It is quite possible that I ought to have given it in larger doses on this occasion.

CASE 12.—The patient, aged 26, a Japanese fireman, was admitted to hospital on Nov. 11th, 1913, with a three weeks' history of dysentery contracted in Bombay. His tongue was moist and covered with a creamy white fur, and he complained of pain and tenderness on the left side of the abdomen. He had 15 motions, containing blood, mucus, and amœbæ on the first day, and 19 motions on the second and third days after castor oil had been administered. On arrival he was at once given emetine injections gr. $\frac{1}{3}$, night and morning, which were increased to gr. $\frac{1}{2}$ six days later. His absence of knee-jerks and abnormal cardiac sounds made me fear that dysentery had supervened upon latent beri-beri. His fæces contained eggs of Trichocephalus dispar and Heterophyes heterophyes. Emetine reduced his temperature from 100° to 99°, and his evacuations from 15 to 8, but

he gradually became more sleepless and exhausted, and died on Nov. 23rd in spite of bismuth, morphia, brandy, strychnia, and ether. His differential count on admission showed lymphocytes 25, large mononuclears 29, polymorphonuclears 46 per cent. At the post-mortem examination by Dr. Newham on the following day the body was generally emaciated, there were œdema of lungs, evidence of old pleurisy on the left side and congested peritoneum, while in the small intestine there were 2000 Heterophyes heterophyes worms, mostly in the jejunum. Upon them Dr. Leiper reported: "They are identical with the Egyptian form, and tally with the classical description by Professor Looss save in one point; the yolk glands are not confined to the lateral aspects of the worm, but clumps are seen at irregular intervals in the central portion among the coils of the uterus." There were almost no dysenteric ulcers above the ileo-cæcal valve, but they were very numerous throughout the large intestine and extended down to the transverse muscular coat; the mucous membrane between the ulcers was greatly swollen, hyperæmic and undermined; in places the wall of the bowel looked healthy, in others it was of a slate colour. The liver weighed 64 oz. and was of a pale colour, of normal consistence and friability, but in the right lobe, 1 inch from the under surface, there was an abscess, about the size of a walnut, containing yellow material, tinged here and there with red. The spleen was triangular in shape and small, weighing only 2⅓ oz. All other organs were normal.

I should add that there was no evidence in this case of complication by bacillary dysentery, and Dr. Wenyon could find no amœbæ in sections of the large intestine, showing, therefore, that emetine had killed them. The whole of this large intestine is here for inspection.

Value of Bismuth.

For 30 years I have been a believer in the empirical use of bismuth (subnitrate or salicylate) during and after the special anti-dysentery treatment, and I still continue to use it as an attendant on emetine. I have found doses of 15 to 60 grains every four hours sufficient for an adult, and have tried to avoid constipation by giving a saline mixture once or twice a week. Dr. W. E. Deeks in Panama for the last six years has successfully adopted the plan of dosing patients by the tea-

spoon (about 3 drachms of bismuth subnitrate) every three or four hours. It was thought at one time that bismuth acted as a direct poison to entamœbæ, because they were found to disappear not only when lying free in the great intestine, but also when buried in the bowel wall. But Dr. S. T. Darling negatived this by culturing free-living amœbæ on media sown with bismuth.

Dr. W. M. James,[17] of Ancon, states that entamœbæ are very seldom met with in the stools after the second day of bismuth treatment, though he once saw them in great numbers on the seventh day. He thinks it quite probable that the action of the hydrogen sulphide of the bowel on the subnitrate may deprive the entamœbæ of an essential element of their food-supply. My own belief in bismuth as a secondary drug has increased since the introduction of emetine, because I notice that the cases of relapse after a few days of emetine which I have seen and read of are those which have not also had the benefit of a course of bismuth. Dr. James finds that if amœbæ are kept for one or two hours in a moist chamber before being fixed and stained certain degeneration forms appear, characterised by disappearance of the nuclear network and collection of the chromatin into large blocks against the nuclear membrane with loss of staining of the karyosome. In patients treated with bismuth subnitrate similar degenerative changes are observed in amœbæ fixed and stained immediately after their passage from the body.

In our present state of knowledge, and until it has been proved that emetine alone will banish the infection for all time, I agree with Dr. James in recommending "the simultaneous employment of bismuth subnitrate in large doses because of the difference of action of the two drugs against the entamœbæ. If there be any emetine-immune entamœbæ resulting from the employment of the alkaloid the bismuth subnitrate will effectually deal with them, and very possibly the latter drug will materially aid in the effectiveness of the emetine, just as mercury must also be employed with salvarsan in the successful treatment of syphilis, even though the action of bismuth is not that of a direct poison, as is the action of mercury."

The general treatment is the same for amœbic and bacillary dysentery, so I will postpone it to the next lecture.

Complications.

The chief complication of amœbic dysentery is abscess of the liver following hepatitis, and it is very much to be hoped that a universal and sufficiently prolonged treatment of dysentery by emetine will eventually lead to an enormous reduction of this complication, which succeeds dysentery, according to various statistics, in from 11 to 33 per cent. of hospital cases. Formerly we used to be thankful if we could put an end to dysenteric symptoms by any treatment, and we then seemed powerless to prevent any extension of amœbæ to the liver in our convalescent patients. Now that we know that emetine kills amœbæ we must be careful that our use of it is sufficiently prolonged to destroy not only the amœbæ in the intestine, but also those which have already been transported by the blood stream to liver or lung. In spite of the fact that I have seen Muhammedan patients who vowed that they had never had any use for alcohol, I still think that free libations play an important part, at least in Europeans, in the etiology of liver abscess. The well-known rarity of the complication among women may be partly explained by their smaller consumption of alcohol, and I have noticed on the very rare occasions when a European woman has suffered from it that she has been endowed with a typical masculine thirst.

Amœbic abscess of brain and spleen are met with occasionally in Egypt. Abscess of the lower lobe of the right lung may occur, and is not always recognised until it is encountered at the necropsy, when the diaphragm is found to be adherent to the liver and pleura. Local peritonitis may result from extension of the bowel ulceration, especially in gangrenous cases, but this is very difficult to diagnose during life. General peritonitis may follow the bursting of a liver abscess or a large perforation of the intestine, which usually occurs in the cæcum and is always fatal. Dr. R. P. Strong[18] found

perforation 19 times in 100 fatal cases, but in 200 of his clinical cases it only occurred three times. Appendicitis, intestinal hæmorrhage, and sprue (in tropical countries) must be mentioned among rare complications, with arthritis as a sequela.

The Danger of Carriers.

The importance of this question in every country has already been referred to while discussing amœbæ, but other papers on the subject have been published since I began writing this lecture. Dr. C. Mathis, for instance, found in Tonkin that 8 per cent. of a limited number of natives examined were acting as healthy carriers of Entamœba histolytica. He believes that direct human contagion is as important in the spread of the disease as the indirect infection by food and water, and quotes in favour of this view the absence of dysentery among troops in barracks and its sudden appearance under the more crowded conditions of camp life, as also the frequent attacks among doctors and nurses.[19]

Professor Landouzy has drawn attention to the occurrence of amœbic dysentery in 14 individuals who have never left France, and suggests that there is a gradual acclimatisation of this disease in that country. His record shows that there have been 7 liver abscesses and 5 deaths. Four of the victims had been directly associated with colonials who had returned from the tropics, but the others apparently had not. He suggests that amœbæ should be searched for in all cases of rebellious diarrhœa of unexplained orgin, even though there may be no blood in the stools. He insists that returned colonials who have attacks of dysentery must no longer be regarded as incapable of spreading the disease.[20]

Dr. E. B. Vedder considers that the presence of a considerable number of these chronic amœba carriers constitutes a sanitary menace to the community, and thinks it possible that they may be rid of their amœbæ by a course of enemata of quinine or silver nitrate [13] when emetine proves insufficient.

Lastly, Dr. S. T. Darling, in reporting a case of

entamœbic colitis naturally acquired in a dog, reminds us that we should bear in mind the possibility of dogs and cats acting as carriers of amœbic dysentery.[21]

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LECTURE III.

BACILLARY DYSENTERY.

WHAT cannot totally be known ought not to be totally neglected, for the knowledge of a part is better than the ignorance of the whole.—Ismail ibn Ali Abu el Feda (Preface to his Geography).

Epidemic dysentery is met with in all parts of the world, particularly in times of war and famine and in crowded institutions, such as lunatic asylums and prisons. Pure cases of it are not amenable to ipecacuanha or emetine, and it is not followed by abscess of the liver. Bacillus dysenteriæ, which includes a group of nearly allied bacilli, is now known to be the cause of the disease, which is therefore termed bacillary dysentery to distinguish it from amœbic dysentery.

BACTERIOLOGY.

The bacilli of dysentery have been isolated from a number of cases of infantile diarrhœa in the United States and in South Africa (Birt), but Morgan failed to find them under similar circumstances in London. In human victims the bacilli are found in the mucous membrane of the large intestine and in the stools, especially in the accompanying mucus. The organism does not become generalised in the blood, but it has been found in the mesenteric glands and once in the spleen. Several varieties of the bacilli have been described, differing from each other in detail and particularly in their action upon sugars. The varieties are usually divided into two types; the Shiga-Kruse, which does not ferment mannite, and the Flexner or mannite-fermenting type. To these two types must be added the Bacillus dysentericus El Tor, described by Dr. Ruffer in 1909, and found then and since to be the

chief cause of dysentery among pilgrims returning from Mecca to the quarantine station at El Tor on the Red Sea coast.[1] It has the characteristics of the dysentery group, but differs somewhat from all the known varieties hitherto described. Ruffer, however, allows that the name is provisional and that his bacillus may eventually be found to be identical with one of the other bacilli. I may remind you that there is a similar multiplicity of varieties of the cholera vibrio, but it seems to me absurd to write about "true" and "false" dysentery bacilli.

Experimental inoculation.—The Shiga bacillus is the commonest cause of this type of dysentery, and is the one a culture of which produced dysentery in Strong and Musgrave's criminal (see Lecture I.). Negative results have, however, usually been obtained by feeding experiments on animals, though the following three successes are mentioned by Besson.[2] Chantemesse fed guinea-pigs with bacilli and produced dysenteric lesions in their intestines; Shiga introduced a culture into a cat's stomach and found that the animal suffered from mucous diarrhœa, with bacilli in the fæces; Kazarinow, by means of an œsophageal sound, introduced quantities of culture into the intestines of rabbits, and thus produced dysenteric lesions. Inoculation of bacilli into veins or into the peritoneal cavity is rapidly fatal, and causes hyperæmia but not ulceration of the intestines. Subcutaneous inoculation of rabbits, dogs, cats, and young pigs is followed by lesions resembling human dysentery and death. The Flexner bacillus is much less pathogenic to animals than the Shiga type, but the Tor bacillus occasions in guinea-pigs and rabbits fever, diarrhœa, paralysis, and death.

Microscopical appearance.—Hewlett[2A] says:—

The bacilli are aërobic and facultatively anaërobic. On agar a thinnish creamy growth develops; on gelatin a white growth nearly limited to the inoculation track, and without liquefaction. The colonies on a gelatin plate closely resemble those of the typhoid bacillus. On potato the growth is either thin, grey, and slightly visible, or thicker and yellowish or brownish. The colour of neutral red media is

unaltered. Litmus milk first becomes faintly acid, then markedly alkaline ; no clotting. Indole is generally not formed (never by the Shiga type) ; occasionally a trace may be detected. All strains ferment glucose with the formation of acid only ; no gas ; none ferment lactose. Some strains (the Flexner type) ferment mannitol with the formation of acid only, no gas ; other strains (the Shiga-Kruse type) have no action on this alcohol.

Agglutination reaction.—As originally discovered by Shiga, the blood of patients suffering from bacillary dysentery agglutinates in dilutions of 1 in 10 to 1 in 100 with the particular strain which caused the infection. But the reaction only appears in severe or moderately severe cases, and not before the end of the first week of illness or even later. It may remain for several weeks after recovery, but as a method of diagnosis the agglutination test has considerable limitations.

Toxins.—Only the Shiga bacillus produces toxin when it has been grown for a month and then filtered.

Detection of the bacillus.—The routine method for detecting the bacillus is to examine a fresh stool, which, if possible, has been passed into a sterile pail and is not mixed with urine. The bacilli are most numerous during the first week of the disease and gradually disappear until the third week, when they can no longer be found. They cannot be differentiated by the microscope alone, and the suspected material must therefore be sown on agar. Dr. P. H. Bahr,[3] in Fiji, found the following method the best :—

A platinum loopful of the blood and mucus was diluted in broth and plated out on Conradi-Drigalski plates ; 8 to 10 drops of the emulsion were found sufficient for one plate. When pure mucus without contamination with fæcal matter was passed by the patient, the dysentery bacilli were on several occasions obtained in almost pure culture. Dilutions and cultivations in MacConkey's bile broth proved unsatisfactory, as the dysentery bacillus appeared to become rapidly overgrown by other organisms of the coli group. On Conradi-Drigalski medium colonies of the dysentery bacillus were recognised by their peculiar transparent blue colour. They were further distinguished by their morphological and Gram-negative characters, and, lastly, by their sugar reactions.

Dysentery bacilli cannot live for long anywhere outside the human body. They die rapidly in sunlight or in ordinary sewage or in distilled water, and experimentally they are rapidly killed off in a broth medium when bacillus coli is added to it, yet for some unknown reason they are able to cultivate themselves in the human intestine.

Post-mortem examination should be obtained as early as possible because putrefaction in the tropics begins immediately after death. To make cultures a loop of the large intestine should be ligatured and removed, when the interior may be washed with sterile water. The mucous surface is then cauterised with a red-hot iron rod, and a platinum loop is plunged through the surface into the subjacent tissue. Dilutions in broth can then be plated out on Conradi-Drigalski agar.

Pathological Anatomy.

The character of the intestinal lesions varies as the dysentery is acute or chronic. In severe cases the mucous membrane of the colon and rectum suffers uniformly and, when ulceration is extended to the small intestine, it is the lower part of the ileum which is usually involved. The acute lesions begin on the projecting transverse folds, and extend to deeper levels; they consist of swelling and necrosis of the mucous membrane with the formation of irregular islands of a false membrane, often of a dark green colour. The ulceration depends in extent and depth upon the amount of necrosis and does not show the regular punched-out lesions of amœbic dysentery. At a necropsy soon after death there is very marked hyperæmia, but this fades in museum preparations. The intestinal contents, of course, resemble the stools before death, and usually consist of tenacious mucus with thick green liquid fæces. In the chronic disease the whole intestine is thick and hard, and islands of ulcerated mucous membrane may alternate with the pigmented, depressed scars of ulcers which are healed. Perforation and suppuration of the intestine occur but seldom.

The microscopical appearances must, of course,

vary with the stage and severity of the disease. The most extensive changes are necrosis of the mucous membrane, where the epithelial cells can, perhaps, no longer be determined. The chances of recovery depend more upon the lesions being limited to the lower gut, even if the ulceration be deep, than to the involvement of the whole of the great intestine and the lower half of the small intestine in acute inflammation of a superficial character. The chief change in the submucosa is thickening from infiltration, and Dr. Bahr[3] noted that where the muscular coat remained intact no bacilli were ever found in the submucosa. Dr. S. Flexner says that the false membrane "is a close-meshed network of fibrin enclosing multinuclear, often fragmented, cells."

Bacteria are abundant in the necrosed mucous membrane, but are not so easily found in sections below it. Many careful observers refrain from determining dysentery bacilli by their morphological characters alone. In the Pretoria Yeomanry Hospital, which I helped to start, there were, in 1900–01, 3782 medical in-patients (British officers and men), among whom dysentery, with 475 cases, came second on the list of frequency. There were 13 deaths or 2·75 per cent. Amœbæ were never discovered by Dr. J. W. Washbourn and others, and in only one case was there a single hepatic abscess. It is fair to assume for various reasons that these 475 cases were all, or very nearly all, of the bacillary type.

Microscopically, the earliest stage seemed to be in the columnar cells lining Lieberkühn's crypts in the colon. Then followed small cell infiltration and œdema of the connective tissue around the vessels between the mucous crypts. The report written by my successors, Dr. Washbourn and Dr. H. D. Rolleston, continues: "The vessels in the submucosa may become thrombosed. The same necrotic process seen in the mucosa may attack the submucosa, and later the inflammatory process may extend right through the muscular tissue into the serous covering or even into fat around the colon. In some instances the muscular layer stains badly, and is broken up, appearances showing necrotic processes. When, after recovery from an acute

attack, death subsequently occurs, the submucous layer is seen to be fibrotic from organisation of inflammatory products."[4]

Clinical Description and Diagnosis of an Acute Case.—Complications.

The incubation period is short—from one to two days. The onset is usually sudden, but may begin with one or two days of diarrhœa. Griping pain in the colon is the first symptom, followed very shortly by motions which consist only of a little blood and mucus. The tenesmus is so constant that the patient is hardly content to be away from the bed pan. The fever in an uncomplicated case is seldom above 101° or 102° F., and does not last for more than three to eight days, while in a mild case the temperature may never be above 99°. The stools may vary in the 24 hours from 12 to 50 or many more. The tongue is slightly coated or may be clean, but there is no appetite for food. A fatal case gradually develops a rapid pulse, cardiac failure, and collapse, in spite of an apparent improvement in the temperature, and in the frequency and appearance of the motions.

In gangrenous or fulminating cases the symptoms are severe from the onset, the stools may resemble washings from raw meat, with large sloughs of necrosed mucous membrane, causing death as early as the third or fourth day. Fayrer, however, records a case in which a slough about a foot long was discharged and the patient recovered. Malaria, scurvy, arthralgia, arthritis, and cicatricial stenosis may all complicate bacillary dysentery. In the Pretoria cases there were two of multiple liver abscess without pylephlebitis. Five out of 11 men who contracted enteric fever, probably due to a plague of flies, from 26 to 70 days after admission to the same hospital, had originally suffered from dysentery. It must not be forgotten that a soldier in war time can contract dysentery and enteric fever at the same time. "Thus a man, aged 21 years, was attacked with dysentery on April 30th, 1901, and was treated for this disease at

Middelburg until May 15th, when he was transferred to the Pretoria Hospital for change of air as convalescent. On admission there his temperature was raised, and he died on May 24th from hæmorrhage due to enteric fever."[4]

Malingering must be borne in mind, for Dr. Bahr found that Indian prisoners in Fiji simulated dysentery in order to escape from labour and get welcome rest in hospital. Sago and arrowroot were added to a stool to imitate mucus; mucus and blood, obtained by pricking the gums, were introduced; one prisoner was seen to add blood and mucus, obtained from another patient's stool, to his own. Others produced diarrhœa "by swallowing large doses of sodium sulphate, obtained surreptitiously."[3]

Malarial enteritis can be excluded by blood examination, by percussing and palpating the spleen, and, if necessary, by giving quinine in proper doses of the proper salts at the proper time of day. It must be remembered that in many parts of the tropics both malaria and dysentery are endemic. Rectal bilharziasis and ankylostomiasis can be discovered by examining the fæces microscopically. The possibility of cancer of rectum in an adult might require digital examination, or the sigmoidoscope.

The differential diagnosis between amœbic and bacillary dysentery is not always so easy as it sounds, especially in chronic cases. It seems to be only expert protozoologists who can be certain of finding amœbæ, and particularly amœbic cysts, in cold fæces. Therefore, a negative report from an ordinary microscopist may sometimes be disregarded, if the patient has been in a dysenteric country, until a week of emetine injections has proved useless. Gentle scraping of the rectal mucosa may furnish evidence of amœbæ or bacilli. Amœbic cases usually run a more chronic and less toxic course than those of acute bacillary dysentery. Professor Rogers, while analysing the most frequent errors of diagnosis in 1000 medical necropsies in Calcutta, found that 12 out of 36 cases of bacillary dysentery were wrongly diagnosed in the wards, but 5 of them had only lived for a day or two after admission to the hospital. Simple diarrhœa and

tubercular diarrhœa were the common errors, and after them, phthisis, acute yellow atrophy of the liver, cholera, remittent fever, and meningitis had been suggested clinically. Individuals returning to Europe from the tropics with chronic diarrhœa are more likely to have the amœbic form, while inhabitants of lunatic asylums and prisons in the British Isles will more probably be infected with the bacillary type.

I have already said that the symptoms and stools of the patient do not furnish us with much clue towards differentiation, but the fæces of a bacillary case are likely to be large, greenish-black sloughs, or they may look like spinach, or be all bright red blood without obvious fæcal material, or they may consist almost entirely of pink mucus. These appearances are not usually seen in the amœbic type. Sprue sometimes precedes or succeeds dysentery, and can usually be recognised by the tongue, history or presence of aphthæ, large, pasty motions, atrophy of liver, and emaciation.

Ulcerative Colitis.

There remains for consideration the vexed question as to whether the disease called ulcerative colitis in this country is or is not bacillary dysentery. The provisional term "ulcerative colitis" originated at Guy's Hospital, and was first differentiated by Dr. Hale White in 1888. It is now generally used in England and is recognised in some American text-books. No one acquainted with both these diseases can have failed to appreciate the resemblance, as regards symptoms and post-mortem appearances, which one bears to the other.

The group of symptoms called dysentery in tropical and subtropical parts of the British Empire is usually labelled ulcerative colitis in the United Kingdom, at least outside lunatic asylums. We are confronted by an illogical outcome, for a case diagnosed as ulcerative colitis in a London hospital ward might be re-labelled if it were discovered later that the patient had lived in the tropics and that his fæces contained amœbæ or

bacilli; or, again, if he became insane and had a colitis relapse in an institution the complaint would be called "asylum dysentery." But sporadic dysentery in this country is not confined to asylums nor to adults, nor to people who have resided in the tropics. Let me recall to your memory the case of a child 2 years old who died in Lambeth in January, 1909, from very acute dysentery lasting only two days. This case was reported by Lieutenant W. E. Marshall, R.A.M.C., who stated that the organism, isolated in almost pure culture, was identified with Flexner's bacillus by cultural and agglutination methods. You may also remember Professor R. Saundby's tinsmith, aged 48, who had never been out of England, in whose stools Dr. J. T. Hewetson found the Shiga bacillus.[5] Dr. H. P. Hawkins analysed 85 purely English cases of ulcerative colitis at St. Thomas's Hospital, of whom 41 died; two of them agglutinated Shiga's bacillus, and in another paper, read before this society, he records an additional case where "from a high rectal scraping B. Flexner was obtained."[6] In 1908 Professor Saundby published a case of a child, aged 3 years, where agglutination with Shiga's bacillus occurred.[7]

The bacteriological research of Dr. Ledingham and others has shown that bacillary dysentery is more widely distributed in England, outside asylums, than has hitherto been believed, and evidence is forthcoming that the bacillus dysenteriæ is occasionally found in the stools of those who were not known clinically to be suffering or to have suffered from dysentery. Some of the strains isolated from such patients, who were suspected of being "typhoid carriers," belong to the mannite-fermenting type of the dysentery bacillus, akin to the one discovered by Flexner in Manila in 1901, and which has since been proved to be the cause of certain epidemics of summer diarrhœa in the United States. Though neither the Shiga nor the Flexner type of dysentery bacillus has been isolated by Morgan, Ledingham, and others from cases of summer diarrhœa in England, it is quite possible that certain sporadic cases of diarrhœa in this country may be caused by some variant of the dysentery bacillus. Too much stress should not

be laid on the fact that tenesmus and pain at the anus, both very prominent symptoms in dysentery, may hardly exist in "colitis," for these symptoms depend chiefly on the site of the ulceration. In any intestinal lesion tenesmus is unlikely to be present if the neighbourhood of the sphincter is not involved. Dr. L. S. Dudgeon, in 1908, unsuccessfully inoculated for Dr. Hawkins two rabbits intravenously and two guinea-pigs intraperitoneally, but have many subcutaneous inoculation experiments on rabbits, dogs, or cats been tried with cultures from the stools of ulcerative colitis patients?

Considering the very high rate of mortality of this disease (70 to 80 per cent., according to Hawkins), its unknown causation and the fact that it occasionally yields to antidysenteric drug treatment (saline purgatives, calomel, large enemata of silver nitrate, &c.), I venture to think that the patient might have a better chance of recovery if physicians would give up their preconceived views. Instead of assuming that cases now called "ulcerative colitis" cannot be dysentery because they have never been in the tropics, how would it be to assume that they are dysenteric, and make every endeavour to find, in early cases, amœbæ, or, what is more probable, some evidence of one of the existing varieties, or of a new variety, of the dysentery bacillus? If this suggestion were adopted the physician might make use of remedies such as emetine and bismuth, or such as a multivalent antidysenteric serum, accompanied by large enemata. If a month of this treatment failed to do any good the patient should be no worse, and the physician could still consider the possibility of employing calomel and opium, or of summoning surgical assistance.

Able physicians, writing on colitis, unconsciously contrast it with the picture of acute dysentery instead of with chronic dysentery, when B. dysenteriæ can no longer be recovered from the stools because they are so outnumbered by B. coli and other saprophytes.

Asylum Dysentery.

I should now like to draw attention to the extraordinary and unexplained prevalence of bacillary dysentery among our lunatics. It seems to linger in some asylums as if it were the last remnant of the dysentery which used to be so prevalent in this country. The Commissioners in Lunacy have still to regret the introduction of dysentery from old asylums into new asylums, built on the best principles of modern hygiene, within a few weeks of their opening. On the other hand, in some asylums dysentery is never present. It is important to note that dysentery in an asylum is not always limited to the insane. The Sixty-seventh Report of the Commissioners in Lunacy, published in 1913, records the existence during 1912 of 1155 cases of dysentery, of which 287 died. There were also 555 cases classified as "diarrhœa or infective enteritis of uncertain origin," of which 64 died. Both dysentery and diarrhœa are slightly more prevalent among female than among male insane patients.

In addition to the lunatics, five members of the staff suffered during the year from dysentery and four women from diarrhœa. These statistics are compiled from 95 county and borough asylums in England and Wales. No less than 72 of these asylums harboured during the year one or more cases of dysentery. In other words, only 24 per cent. of these asylums are free from dysentery. The highest incidence was as follows:—

London: Colney Hatch	53 cases.
Long Grove...	50 ,,
Yorkshire: Wakefield	78 ,,
Devon	90 ,,
Sussex, East	75 ,,
Staffs: Burntwood	69 ,,

These are all asylums with more than 1000 inmates.

In Devon Asylum there were on the inspection day 1311 patients. The heaviest incidence of dysentery was in the autumn months; there were 20 deaths. The Commissioners report that plans

for a pathological laboratory have been approved by the Secretary of State. At the inspection of the East Sussex Asylum after an interval of 20 months the Commissioners report: "During the period under review as many as 191 patients (134 males and 57 females) and two nurses have suffered from dysentery, as regards eight of the patients with fatal termination. At the present time (Oct. 5th, 1912) four patients are in bed with the disease in an active form." They had little else to say about dysentery, but among other benevolent remarks they said "we thought more attention might have been paid to the warming of the plates" at dinner time! The Commissioners do not seem yet to have grappled with their dysentery problem on any modern scientific lines, but they have the grace to acknowledge that "there is certainly no evidence yet of that steady decline we should like to be able to record." Though they recognise the importance of diagnosis and segregation, there is no word in their voluminous report about the danger of human carriers.

It seems to be generally accepted by bacteriologists that all this asylum dysentery is of the bacillary type. Dr. Eyre, working with material from one of the London County Asylums, found not only that a bacillus identical with Shiga's bacillus could be isolated from the stools of six dysenteric patients, but also that the blood serum of some of these patients possessed a specific agglutinative action when tested "against other strains of bacillus dysenteriæ isolated from cases of dysentery in tropical countries."[8] Flexner's bacillus was found in the stools of 17 out of 19 cases of dysentery occurring in the Somerset and Bath Asylum.[8A] Dysentery in the form of local epidemics was well known in England until the middle of the nineteenth century, a date when the first batch of lunatic asylums had already been built. Mr. H. S. Gettings has traced the history of dysentery in the Wakefield Asylum from the month when it was opened, November, 1818, to the present time.[9] By a table, compiled from the case books and registers of the asylum, he is able to shew that dysentery has been present every year for 96 years, with the exception of nine not con-

secutive years, when there is no certain evidence of its having existed. The disease was not always called dysentery; it was often labelled chronic diarrhœa, feverish diarrhœa, dysenteric diarrhœa, and, since 1886, catarrhal enteritis, catarrhal ulceration of the large intestine, influenzal colitis, or ulcerative colitis.

In 1838 Dr. Caleb Crowther, of Wakefield, wrote a book containing a chapter headed, "Is the Spread of Dysentery in our Lunatic Asylums a Necessary Evil, or is it the Effect of Negligence on the part of the Medical Superintendent?" In this chapter he says: "I am firmly convinced that when dysentery spreads by infection in an asylum it is the result of inattention and negligence." Gettings states that when Dr. Bolton was appointed superintendent in 1910 he ordered that the intestines should be opened and examined at every necropsy. "The routine performance of this led to the detection of cases which would otherwise have been missed. It also revealed many cases to be still active that clinically had given no signs for weeks or even months. Before this time it had been the exception to open the bowels, and it is rare to find any note in the (recent) post-mortem books other than 'stomach and bowels normal to external appearances.'" Lunatics are even more difficult to deal with than sane patients, for they may never complain of diarrhœa nor any other intestinal symptoms, and yet when they die they are found to have had, perhaps for years, chronic disease of the colon. Thus it is possible by careful searching, as in cholera and in enteric fever, to detect a carrier who has never been suspected of dysentery, but who has nevertheless been responsible for a localised ward epidemic. Mr. Gettings tells me in a private letter that in 1913 there were 100 cases of dysentery with 29 deaths at Wakefield. Eighty of these were examined by him, and he found the B. dysenteriæ in half of them. It belonged to the Flexner group.

Military Campaigns.

Shiga says of bacillary dysentery, "Always a constant companion of war, it has been more fatal to armies than powder and shot." In the Russo-Japanese war dysentery bacilli were found in Manchuria, in Korea, and among the Russian troops at Port Arthur.

Danger of Flies and Carriers.

Though dysentery in cool climates has not always been, and is not now, confined to the summer and autumn, when house flies are abundant, it is significant that temporary outbreaks both in Europe and the tropics often occur during the fly season. Dr. Bahr has suggested that the fly season in Suva corresponds exactly with the annual epidemic of bacillary dysentery.[3] In many of the Fiji islands "the traveller becomes covered from head to foot with these insects immediately he ventures outside his lodging, and in the sugar districts life is made endurable only by the provision of flyproof netting over the doors and windows." Bahr succeeded in isolating Shiga's bacillus from the lower intestinal tract of flies which had been caught on the bed of a patient suffering from a very acute attack of dysentery and from whose stools the Shiga bacillus had been isolated. He suggests that the flies had imbibed the infection from the soiled clothing. During some 40 experiments conducted later at the London School of Tropical Medicine he found that it was impossible to recover the dysentery bacillus from the intestine of any fly after the fifth day of infection. Also he was unable to obtain any evidence of the multiplication of the bacilli in the flies.[10] But his valuable work, often conducted under trying circumstances, fully justifies our continuing to suspect the house-fly (Musca domestica) as being a carrier of bacilli from fæces to food. This is another similarity in the etiology of dysentery and enteric fever, for every year evidence

is forthcoming which puts the causation of these two diseases on similar lines.

Contamination of drinking water or of raw vegetables, milk, and other food supplies must first be suspected, especially if a group of people are simultaneously infected; but for sporadic, isolated cases, when no evidence can incriminate water and food, we must suspect flies and, what is of greater importance still in every climate, the human carrier. To stamp out dysentery from an asylum or a district it is necessary to treat it with exactly the same precautions as a careful sanitarian devises against cholera or enteric fever. Seven years ago Shiga wrote: "The most important source of infection is the individual suffering from dysentery."[11] In every epidemic there is evidence of contact infection from stools or from the clothes or other articles soiled by the patient.

Gettings is sure that at Wakefield it is the human carriers, the chronic cases, "who keep the asylum infection going, who originate fresh cases and epidemics. They form the keystone of the problem, and must be detected and isolated before any permanent good can be done."[9] Dr. Macalister found, "at a large lunatic asylum in the Midlands," that the actual carriers were chiefly among the incomplete convalescents from dysentery.[12] Tebbutt in the same asylum found, while examining the stools of 28 cases, eight lunatics who were "excreting dysentery bacilli, which were not found necessarily associated with blood and mucus," but he could not discover any bacilli in the flies.[13] In India most of the prison dysentery is bacillary, and Forster, Gillitt, and others have greatly reduced its incidence by instituting "post dysenteric gangs," in which prisoners are isolated after the active symptoms of the disease have disappeared.

Two recent instances of infection may be quoted. In the summer of 1913 an epidemic of bacillary dysentery broke out in a cavalry regiment in Würtemberg, where dysentery had been practically unknown among the troops for several years. The infection was introduced by visitors from Alsace, where dysentery is endemic. There were 52 men infected, no fatal cases, the same bacillus wa s

isolated in every instance, and amongst the apparently healthy men of the regiment no less than 13 were found to be carriers of the same bacillus by bacteriological examination of their stools. After six weeks the epidemic was stamped out without any spread to the other regiments of the garrison.[14] In a children's ward in a Frankfort hospital there were 23 patients, of whom 20 contracted bacillary dysentery and 6 died. The disease was introduced by a child suffering from whooping-cough.[15] There are instances of the disease having occurred among monkeys, and on one occasion it was transmitted from the animal to man. Spontaneous (Flexner) dysentery broke out among monkeys in a Paris laboratory in 1905.[16] Several similar cases developed in 1910 in the animal house of the Bureau of Science in Manila.[17] In 1911 a keeper at the Hamburg Zoological Gardens contracted Shiga-Kruse dysentery while nursing a chimpanzee, which eventually died of that disease. A second chimpanzee from the same cage also caught the disease, and, like the keeper, recovered.[18]

Treatment.

The treatment may be divided into the care of acute and chronic cases and the administration of serums. There are a few general remarks which apply to all cases. Absolute rest in bed is just as important as in enteric fever, but if there is much nausea it is a mistake to lie on the right side. The patient's abdomen must be safeguarded by a flannel belt together with a pad of cotton-wool if the climate permits. A thin linseed poultice, on which have been sprinkled 30 drops of liquid extract of opium, seems to relieve intestinal pain better than a poultice without opium; this can be noticed even in cases where the patient is unaware that opium has been added. The poultice must be very light in weight, because the abdomen is so tender in acute cases.

The diet should be liquid and tepid; albumen water, rice water, to which boiled or peptonised milk may gradually be added. Some patients take Horlick's malted preparation better than any plain

milk; panopeptone and Benger's food are very useful. When convalescence is beginning the food should be very gradually increased, as in typhoid fever, the appearance of the motions, which must be examined every day, being the surest guide. Turkish and Egyptian patients dislike milk very much, and seldom take it in health unless they consider they need an aperient. For them, and very often for all dysenteric patients, the sour milk of Eastern countries, *yaghurt*, is much to be preferred. It is vastly superior to the curdled milk prepared from so-called lactic acid tablets. I see that a preparation called "yaourt" is now for sale in London, but I do not know how it is prepared. The following description of the *yaghurt* used at El Tor is given by Dr. Willmore and Dr. Savage.[19] Several samples of ordinary sour milk were inoculated into sterilised milk. "That which gave the softest and most homogeneous curd was then plated out on MacConkey or lactose cochineal agar, and pure cultures obtained of a large lactic-acid-producing bacillus and a long streptococcus (? S. lebensis). These were then inoculated into sterilised milk (Natura brand)—the Australian condensed milk is unsuitable—and each batch of *yaghurt*, prepared in covered sterilised jars in an incubator at 37° C., was inoculated with a flamed spoon from the preceding one." Alcohol should not be given unless the patient is in a state of collapse, when intracellular saline injections are also useful. Thirst can be alleviated by weak sulphuric acid lemonade. Constipation, when present, can be treated with paraffin or laxamel.

Drugs.

On the first day small doses of calomel help to clean the tongue and the intestinal canal, say, one-sixth of a grain, with a little bicarbonate of soda every hour for six or eight hours. Opium is of no use except as a temporary measure to procure sleep. The saline treatment originally recommended by Professor R. Bartholow in 1877, then of Ohio and later of Philadelphia, often gives good results after the calomel; a drachm of sodium sulphate or of magnesium sulphate can be given

every hour for one day in water with tincture of cardamoms, and subsequently every four or six hours. Its chief use is to empty the intestine of fæcal matter. Tenesmus can be relieved by suppositories of cocaine, belladonna, or opium.

The only large enema I should now use is a soothing one of 2 pints of warm water, in which an ounce of linseed has been allowed to soak for some hours; this may be retained by the patient as long as he likes. If the anus is very sore it may be painted with cocaine before the tube is inserted, or a suppository of 1 grain of cocaine may be introduced half an hour beforehand. Sulphur was given with success during the South African war by Dr. G. E. Richmond in doses of 20 grains, together with 5 grains of Dover's powder. This was ordered every four hours, but in chronic dysentery sulphur alone was given.[4 20]. Cyllin given by the mouth is a useful disinfectant. In chronic dysentery I have faith in bismuth in doses of not less than 15 grains every four hours, and I still have confidence in large enemata of nitrate of silver or sulphate of copper.[21] Professor Rogers has this year published a note of praise of organic silver salts. Those which he thinks should be investigated as being bactericidal to the dysentery bacilli are albargin or silver gelatose, nargol or silver nucleate, and protargol. He finds that boracic acid and quinine have little or no action on the bacilli, but he recommends a further trial of cyllin.[22]

The routine method is to employ a long tube and funnel, or a reservoir containing three pints of the solution 1 in 1000. The rectal tube must be soft to avoid injuring the bowel, and after being well greased with boracic ointment it should be introduced, if possible, its whole length. The solution is not injected but allowed to run in very slowly during some minutes, while the patient is in the knee-elbow position. The tube should be passed by the medical attendant. All patients can hold one pint, rapidly increased to two pints, and some can gradually accustom themselves to take four pints or more. This enema need not be retained for more than five minutes and need not be repeated more than once a day.[21] I used to give in addition, once a day, a boracic acid (one ounce

and a half) and starch enema of two pints, but I once found that an English patient, 12 hours later, was covered with an erythematous scarlatiniform rash over face, inside of arms, abdomen, and legs; and at the margins of this rash, which lasted for 30 hours, were patches, erythematous and slightly raised, ¼ inch in diameter. This patient had retained the enema for 25 minutes and, unlike other patients, he had vomited three times after it. I then treated him with large enemata of saline solution and sulphate of copper, which caused him no discomfort.

Serum.

We know from Shiga that antidysenteric serum is bactericidal as well as antitoxic. Many observers elsewhere have agreed with his verdict in Japan: "The course of the disease is shortened in those who recover and lengthened in those who would otherwise die." During the Tor season, between November, 1912, and January, 1913, there were 16,551 pilgrims who passed through the quarantine station. There were 75 admissions into the hospital with dysentery, of whom 9 died. There were 26 of these cases in which bacillary infection only was present; 22 of them were treated with serum and 2 died, a mortality of 9 per cent. The remaining 4 were not treated with serum, and 2 died, a mortality of 50 per cent. The total dysentery death-rate among pilgrims has been reduced, since the introduction of serum, from 53 and even from 70 to 12 per cent. The routine treatment described by Willmore and Savage is as follows: On admission to hospital of a suspected case a few drops of blood were taken from the median basilic vein and the fæces were examined microscopically and plated out. According to the data furnished by blood reactions and the stool plates, serums were administered, generally multivalent, unless Shiga's bacillus alone was isolated. "The best results are obtained from the administration of very large doses, from 80 to 120 c.c., injected either deeply into the subcutaneous tissues of the flank and abdomen or intravenously." It will be noted that these doses are much larger than the 20 c.c. recommended by the Lister Institute. The injections "are re-

peated twice daily or at longer intervals, as the patient's condition demands, during not longer than ten days after the first dose." The first result of a large injection is a general improvement in the patient's condition, so that occasionally a man, apparently moribund before the injection, may a few hours later be enjoying a meal.[19] Dr. Bahr's recent experience of treatment in Fiji is that the cases injected intravenously with polyvalent anti-dysenteric serum gave the best results as far as could be ascertained.[3] He gave to adults 20 c.c. and to children 10 c.c. or less.

I may conclude by saying that in any case of doubtful origin the combined treatment of the patient by emetine and by polyvalent antidysenteric serum is, in my opinion, both rational and humane.

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